

Fig. 1A

0996056-442704

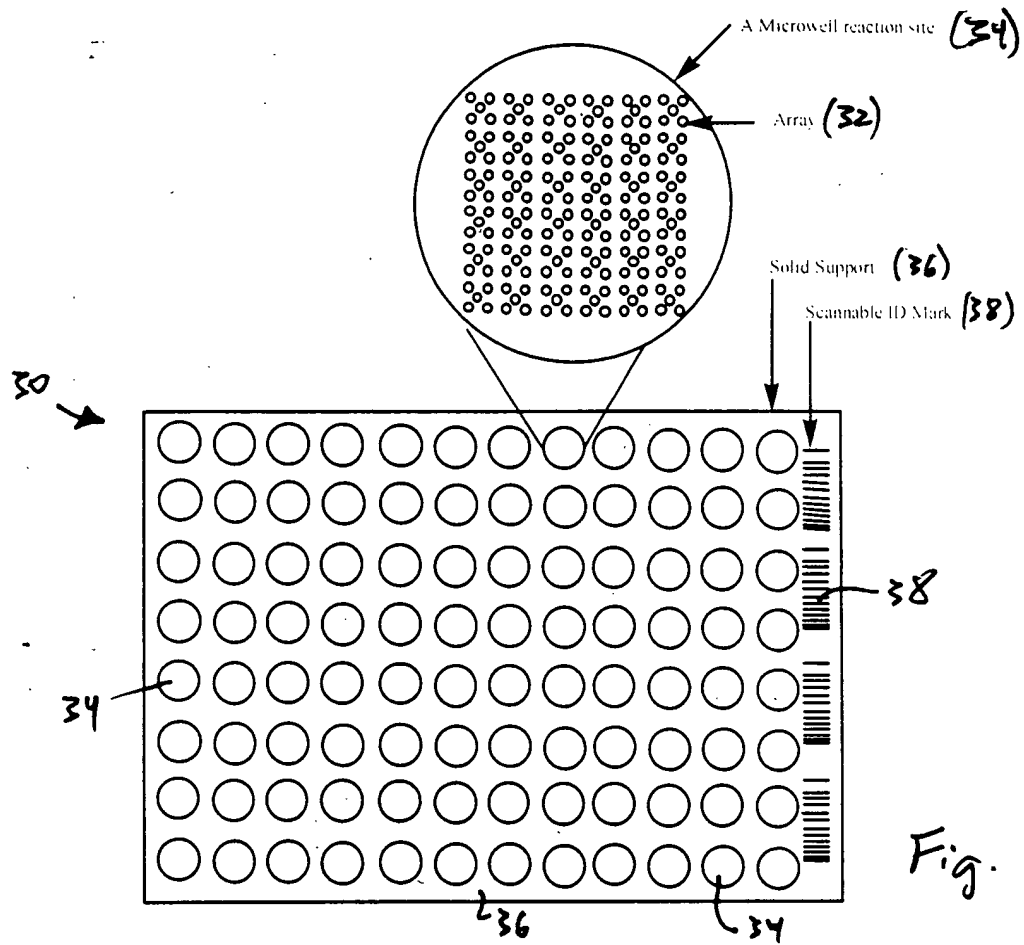


Fig. 1B

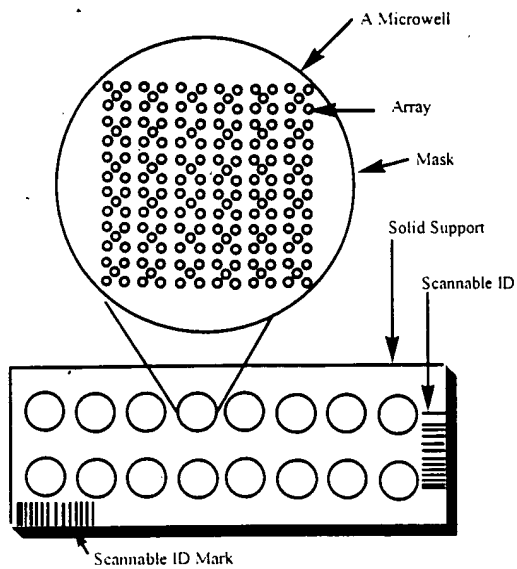


Fig. 2A

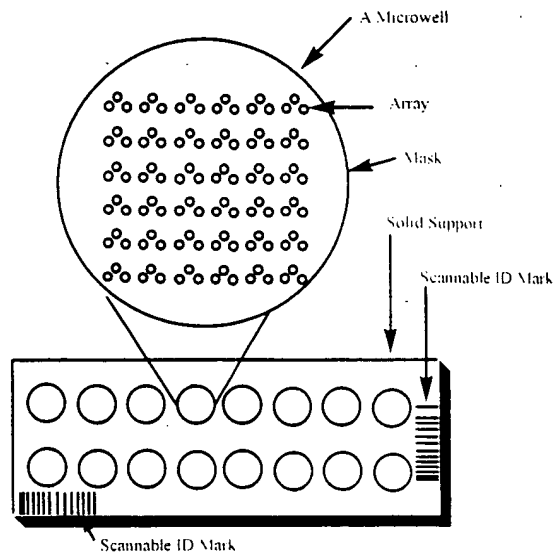


Fig. 2B

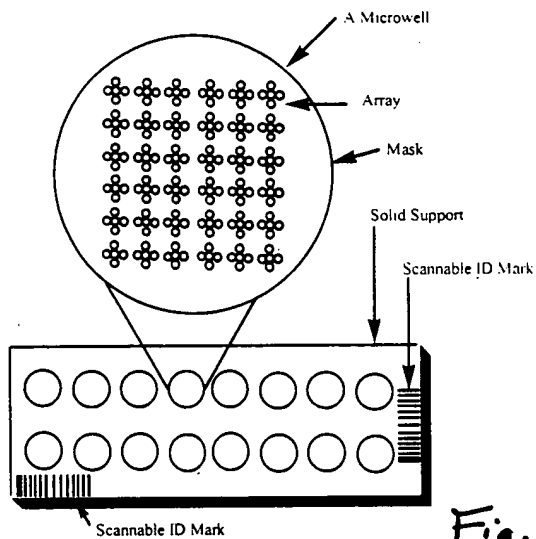


Fig. 2C

Fig. 3A.

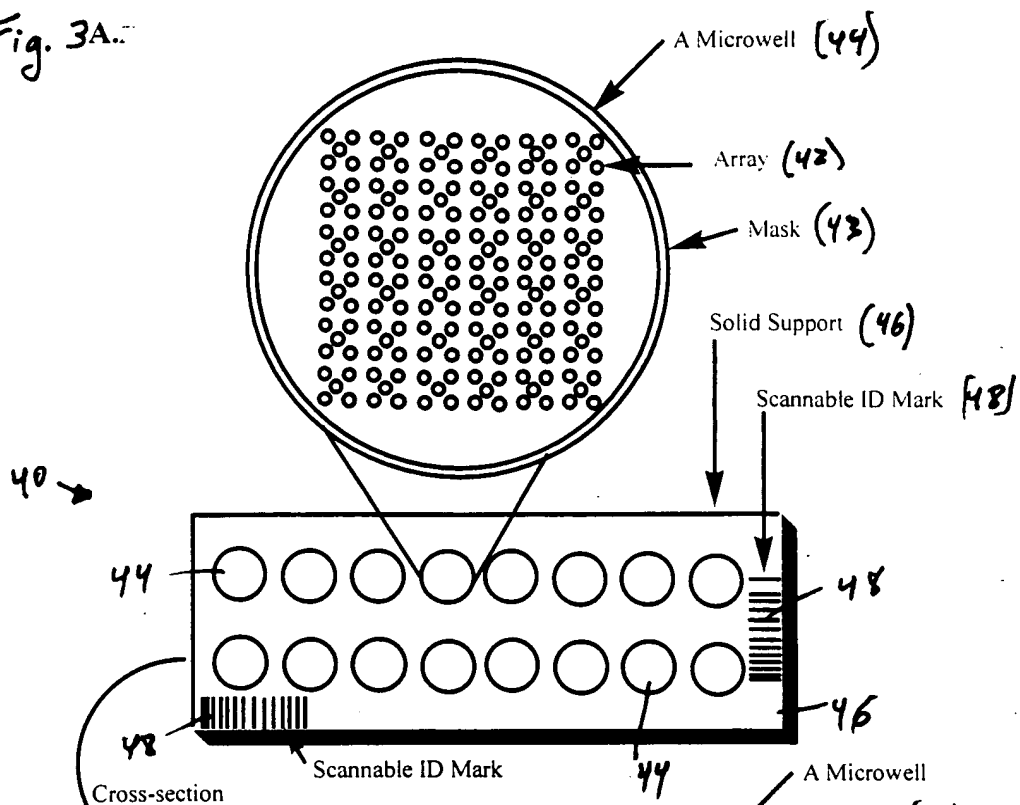


Fig. 3B.

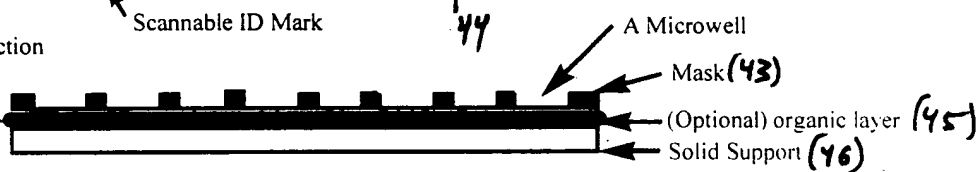
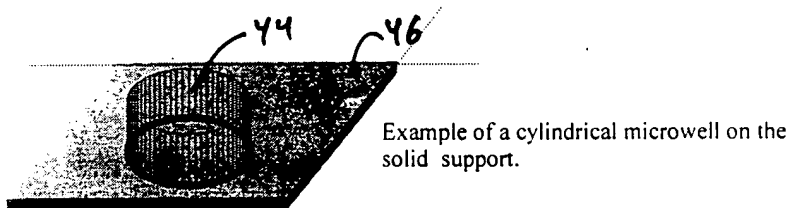


Fig. 3C.



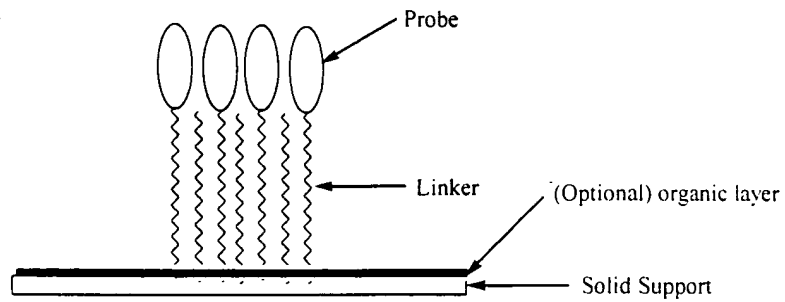


Fig. 4A

A. Attaching probes to solid-support with linkers of same length results in lower density of probe attachment.

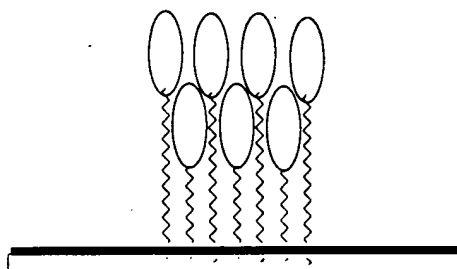


Fig. 4B

A. Attaching probes to solid-support with linkers of different lengths results in much higher density of probe attachment.

TOCTF-9000000

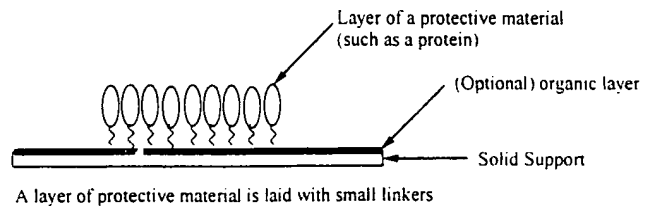


Fig. 5A

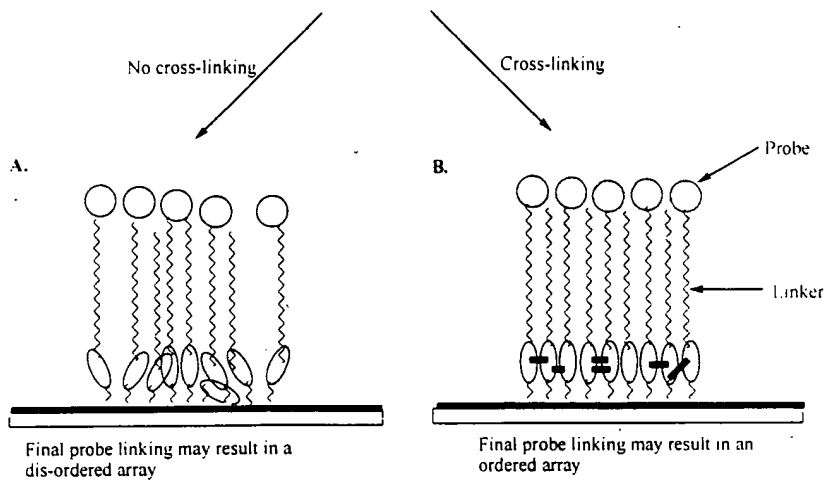


Fig. 5B

Fig. 5C

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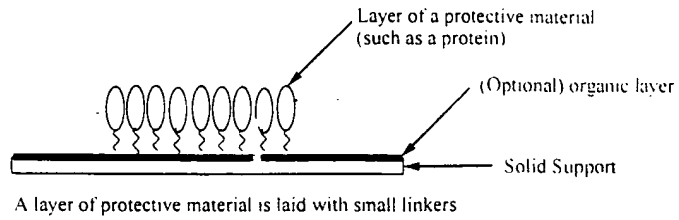


Fig. 6A

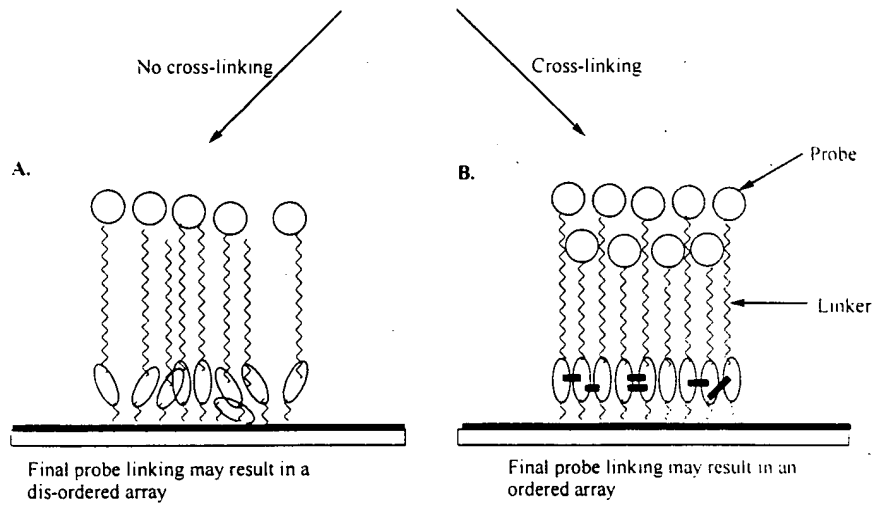
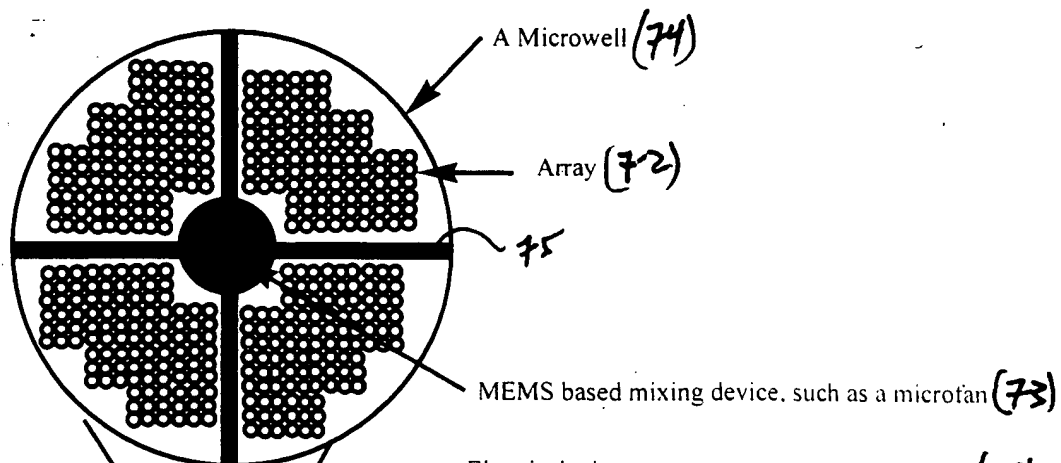


Fig. 6B

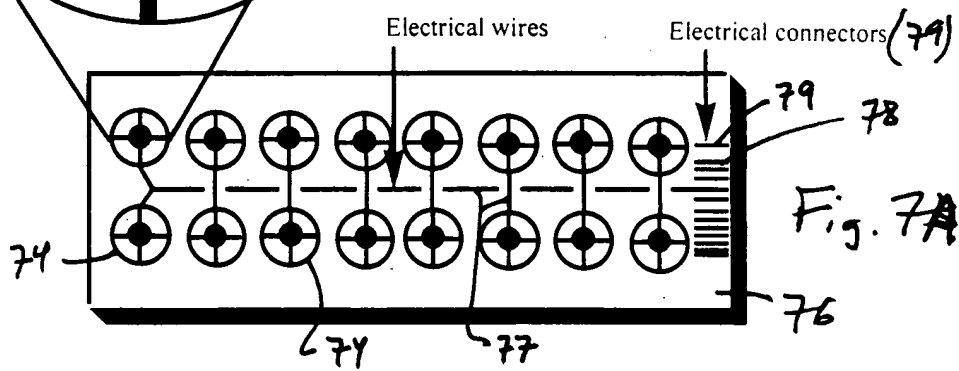
Fig. 6C

0956056-143704

Fig. 7B



70 →



THE FUTURE OF THE FUTURE

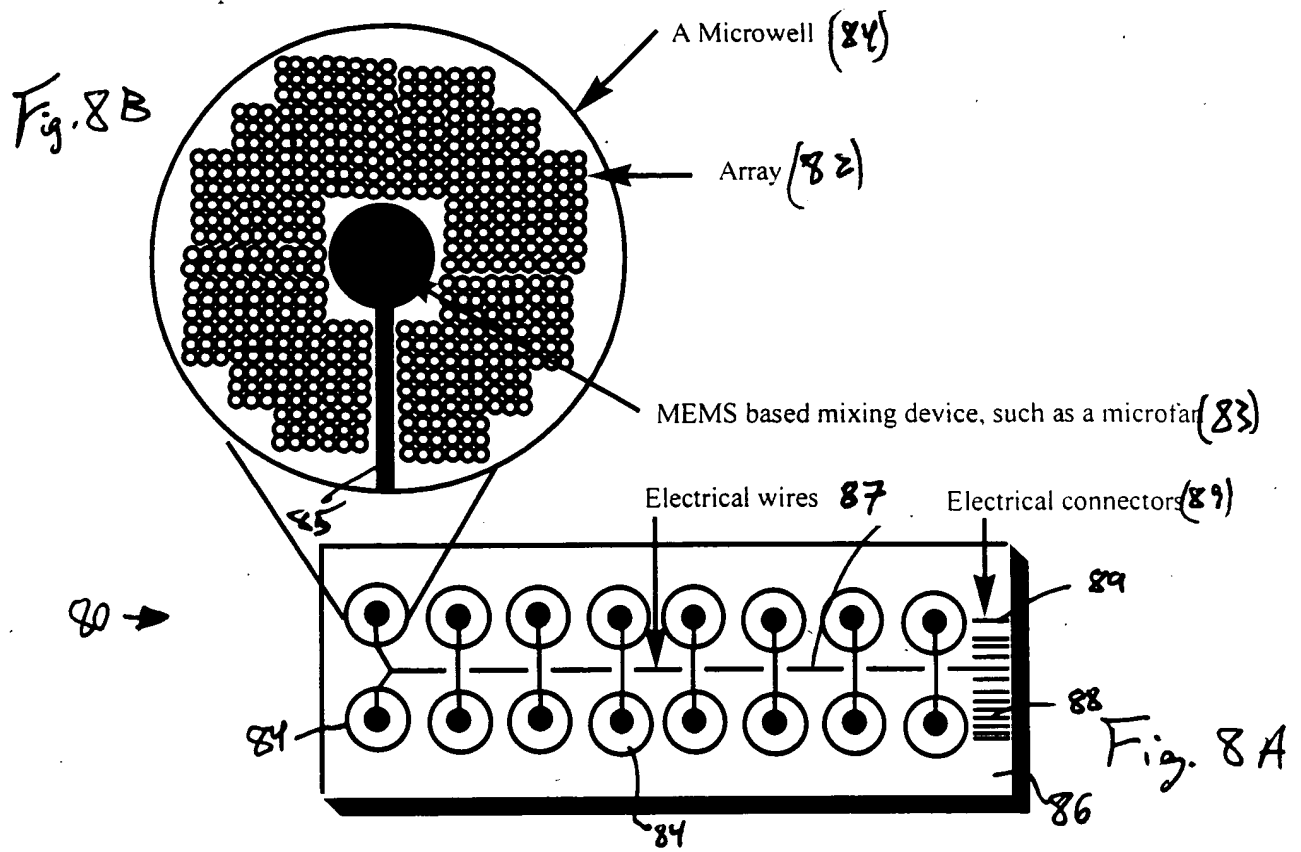


Fig. 9A.

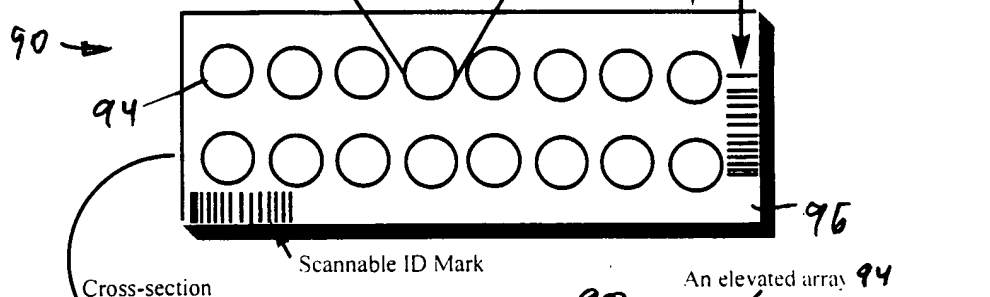
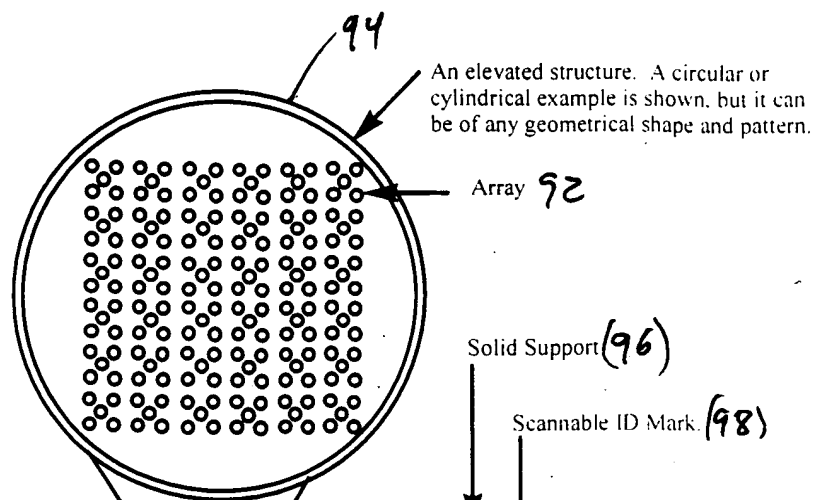


Fig. 9B.

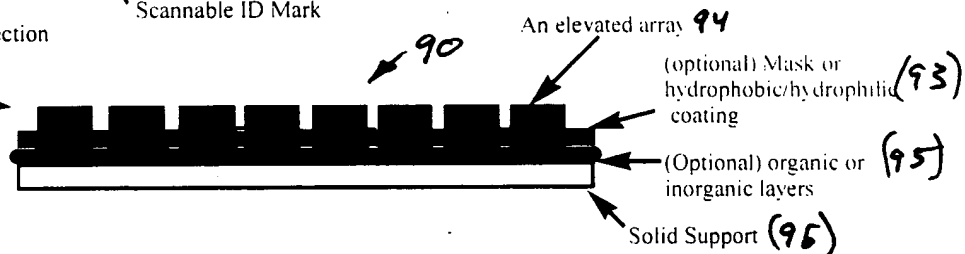
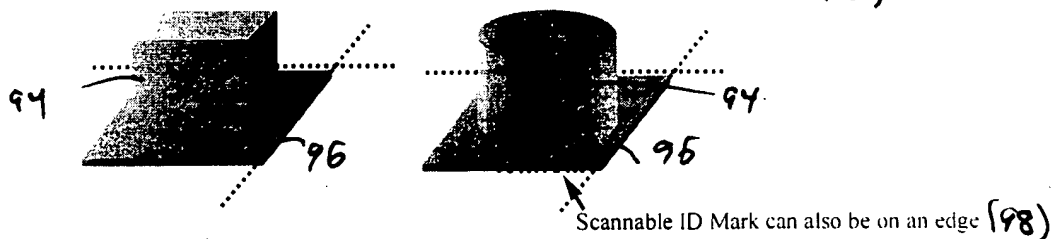


Fig. 9C.



Examples of elevated structures on solid support. The structures can be cylindrical or cuboid or any other geometrical shape.

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Each elevated structure contains a probe array

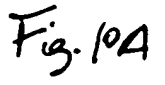
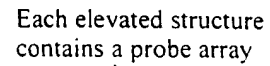


Fig. 10B

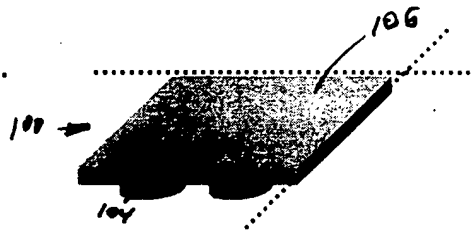
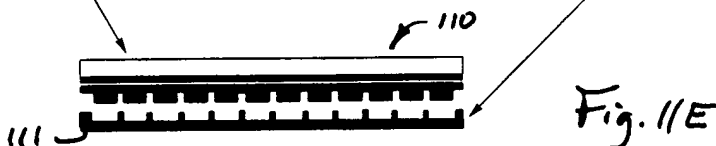
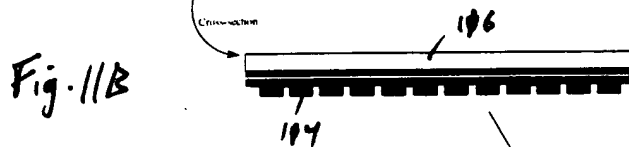
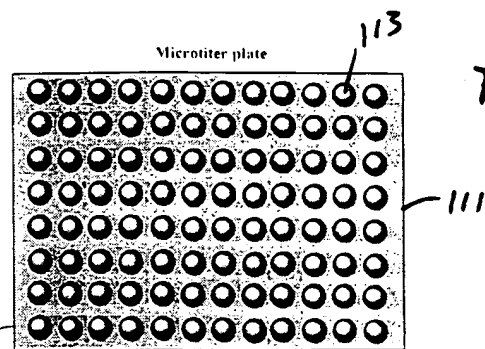
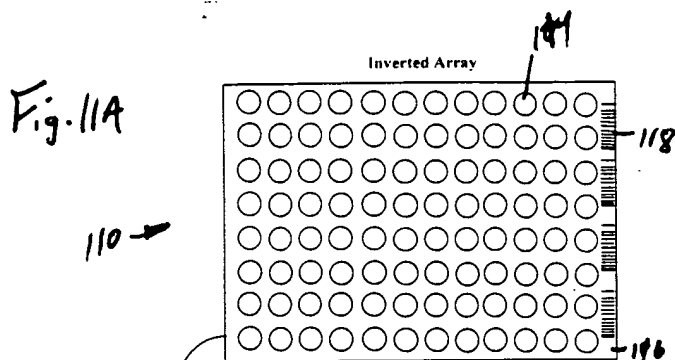
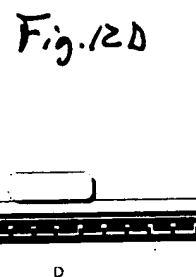
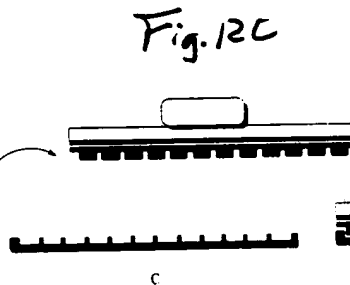
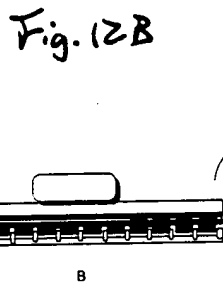
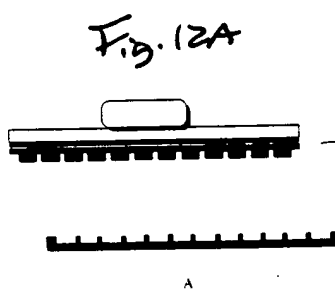


Fig. 10C

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An example sketch showing how an inverted array can fit into a microtiter plate.



The "Inverted Array" can be moved from one reaction vessel to another. It can be moved either using a built-in handle or using a vacuum suction device or any another mechanism. The process can be done manually or robotically and the assay procedure can be easily automated. This schematic shows an example of one such process.

Figure 13A.

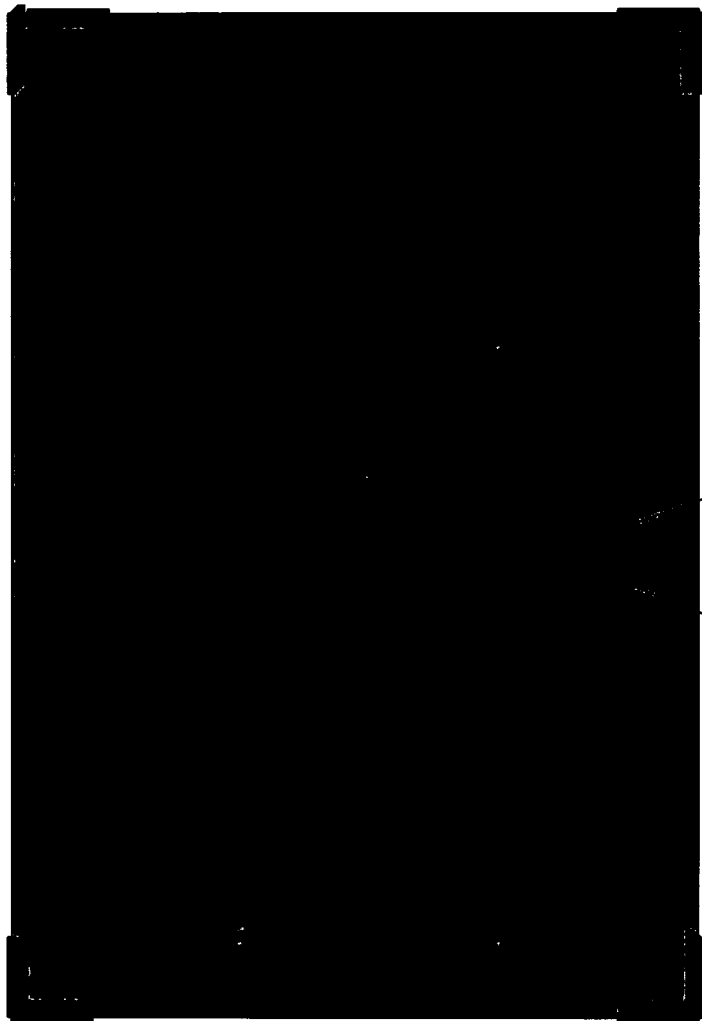


Figure 13B.

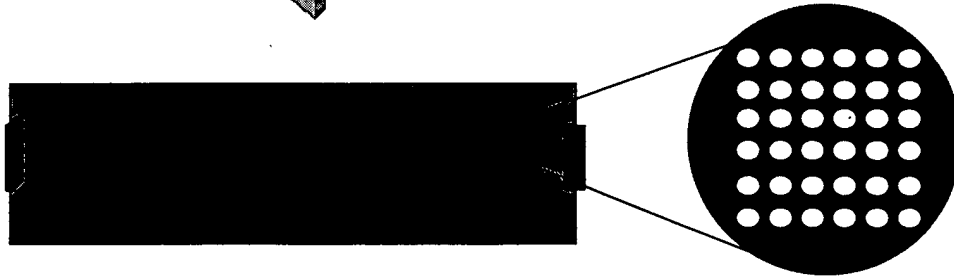


Figure 13C.

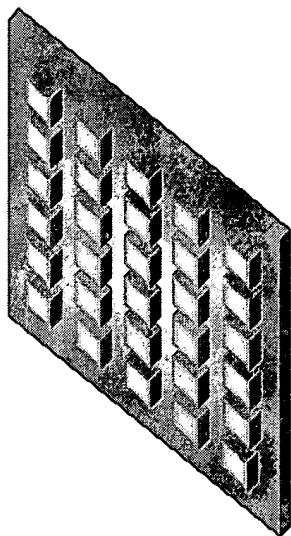
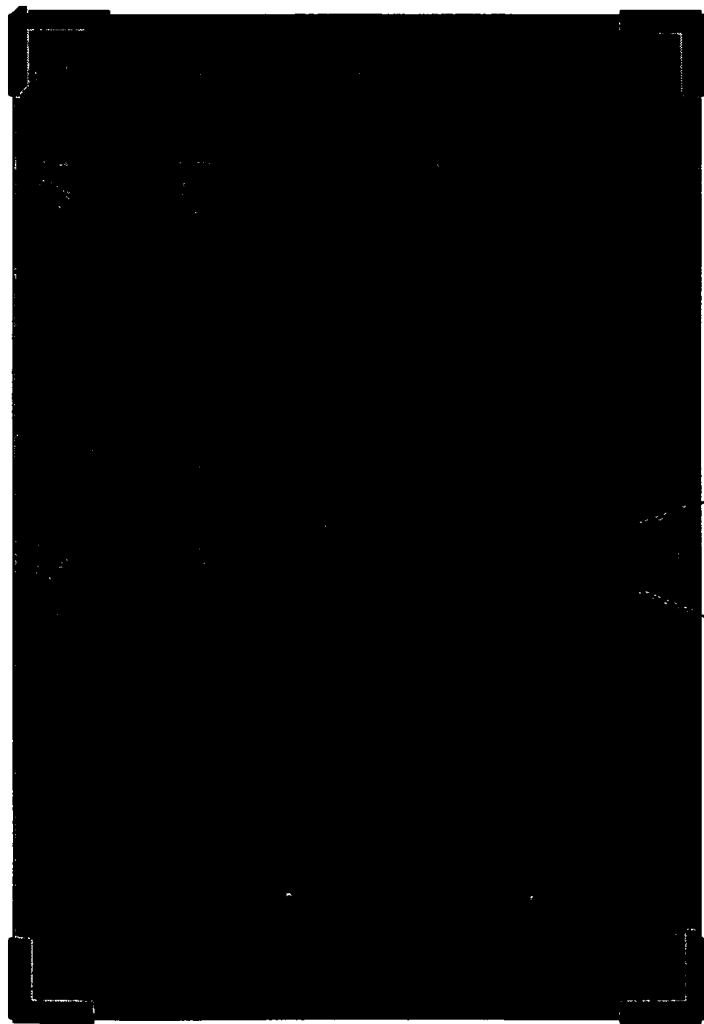


Figure 14A.



Cross-
Section

Figure 14B

Elevated sub-structure

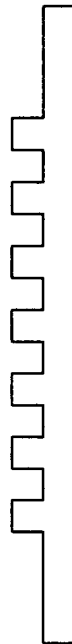


Figure 14C

Planar sub-structure



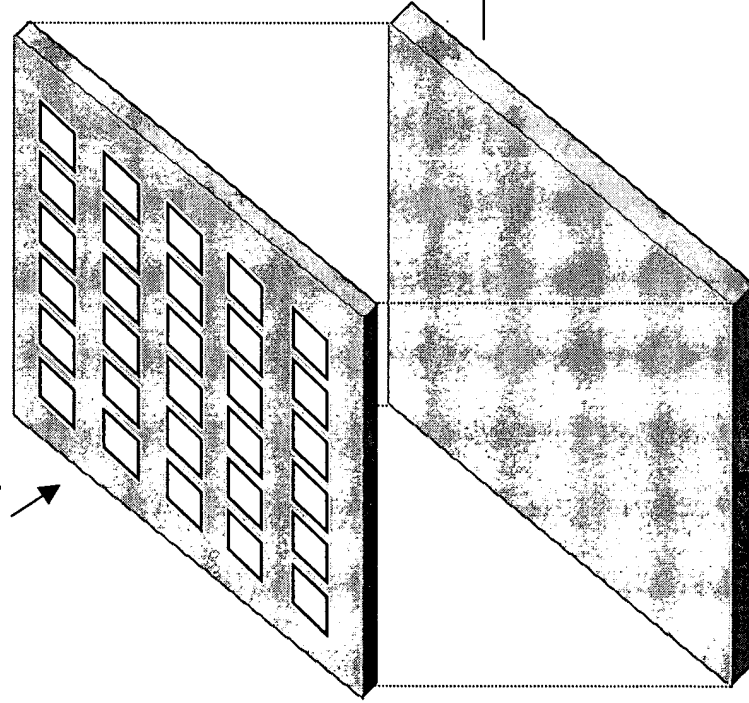
Figure 14D

Depressed sub-structure



Figure 15A.

A three-dimensional substrate with an array of holes.

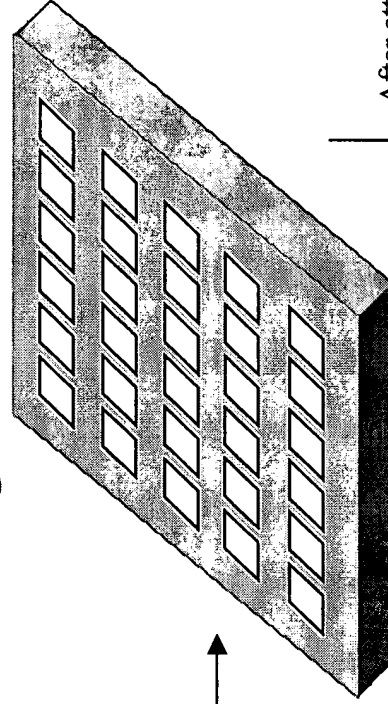


A coated base-plate.

The coating helps prevent attachment of probe-polymer mixture to the base-plate.

The substrate is placed on the coated base-plate.

A mixture of probe and pre-polymer is dispensed into each of the holes



After attachment of the probe-polymer mixture, the base-plate is removed.

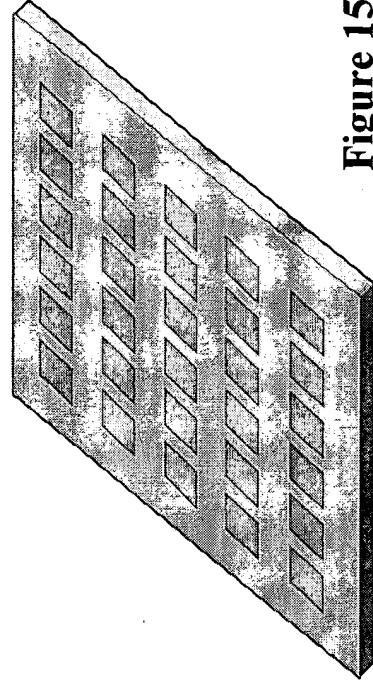


Figure 15C.

Figure 16A.

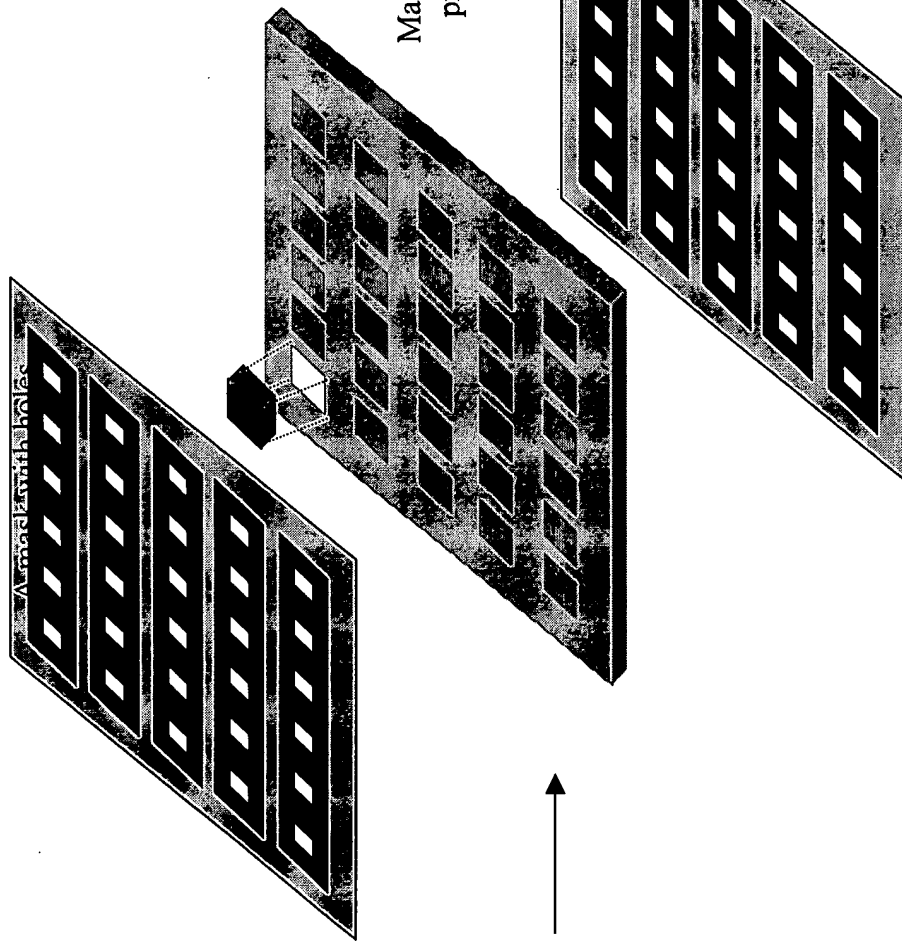


Figure 16B.

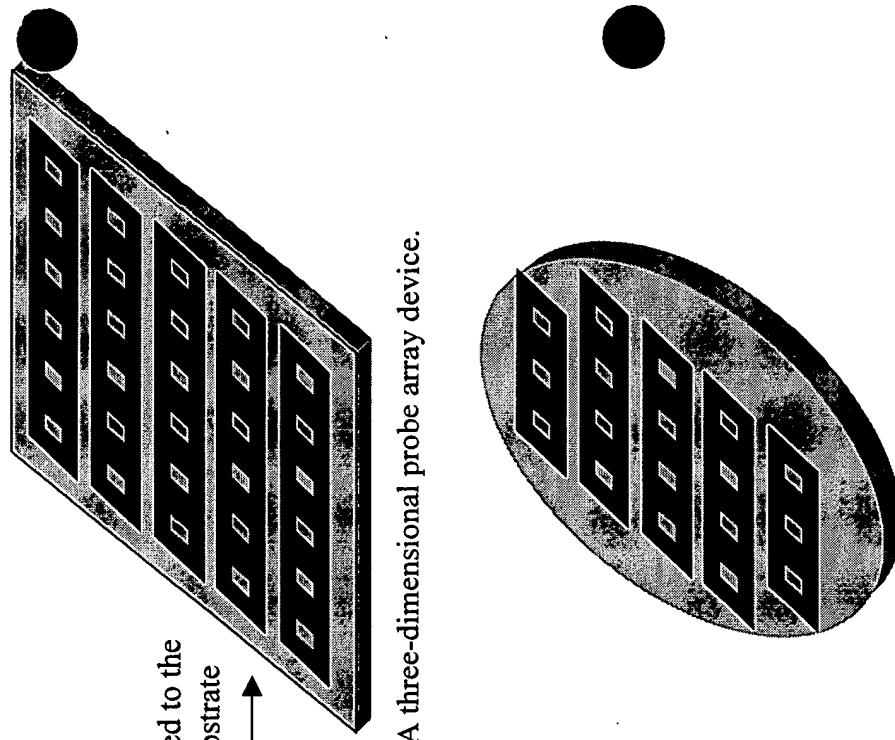


Figure 16C.

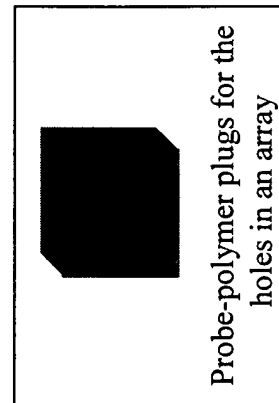


Figure 17.

The microarray biochip can
Also be housed in a sealed chamber.

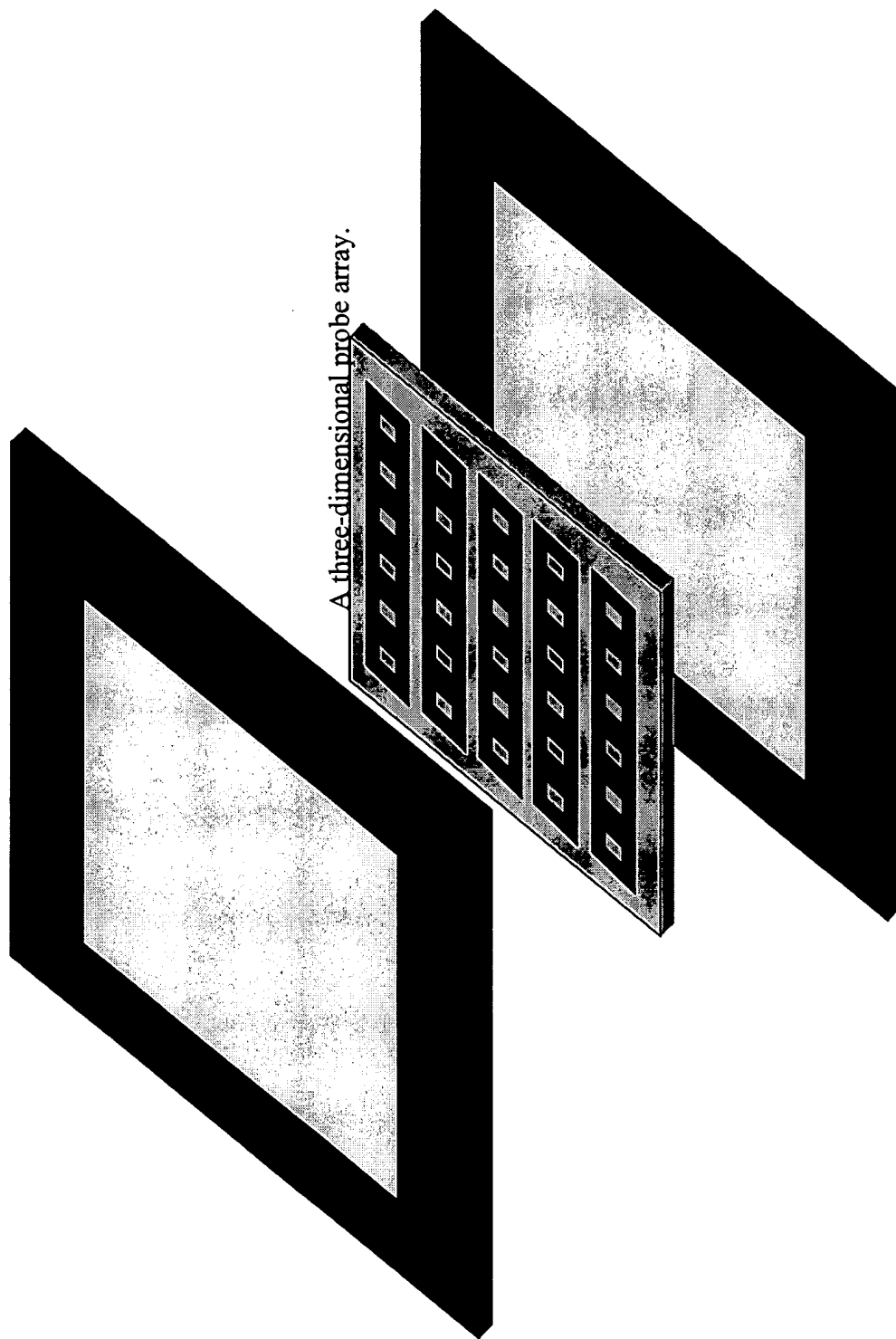
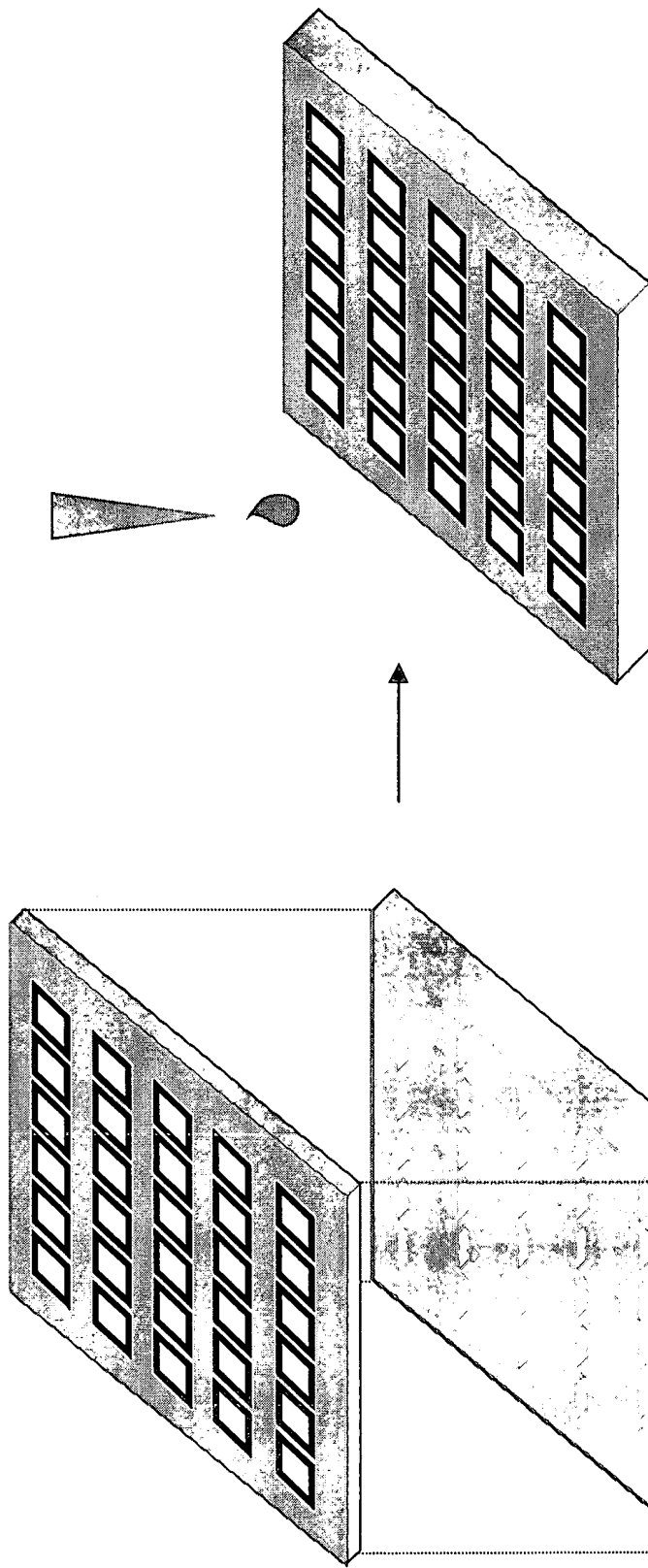


Figure 18A.

Figure 18B.



A coated base-plate with depressions or chambers to hold fluids.
The coating helps prevent attachment of probe-polymer mixture to the base-plate.

Figure 19A.

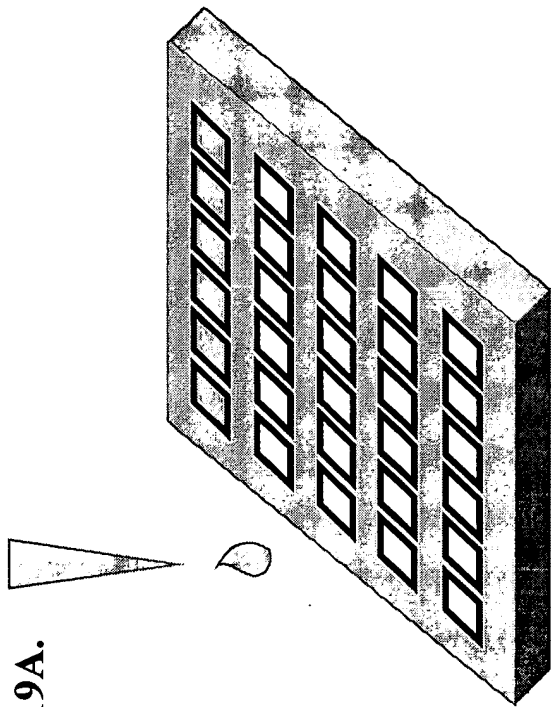


Figure 19C.

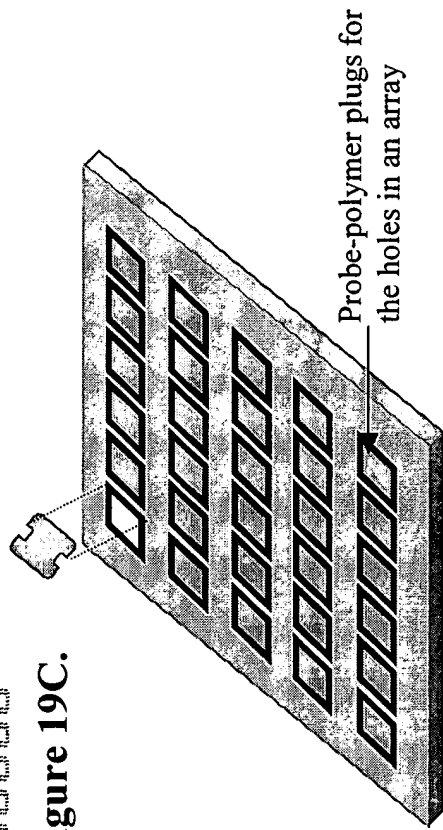


Figure 19D.

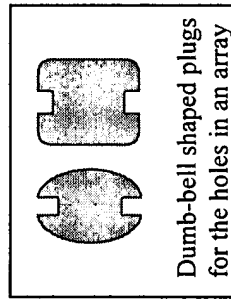
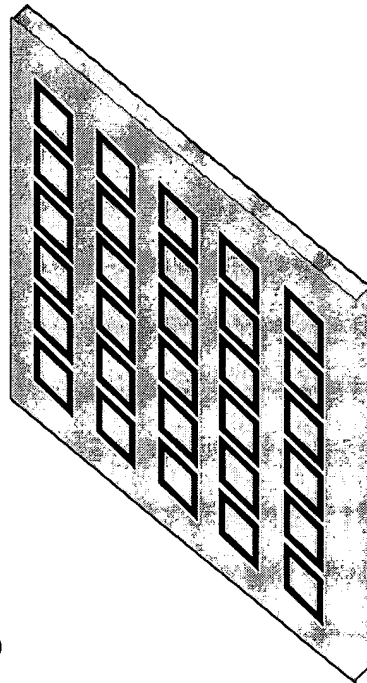
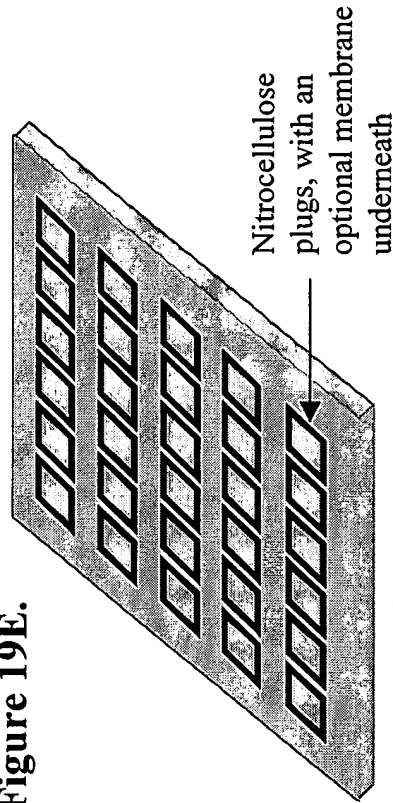


Figure 19B.



Another implementation of 3D porous biochip

Figure 19E.



Two examples of the types of material that can be used to manufacture the 3D porous array

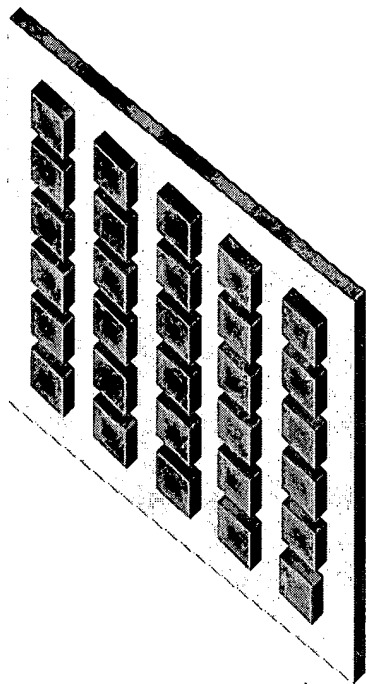


Figure 20A.

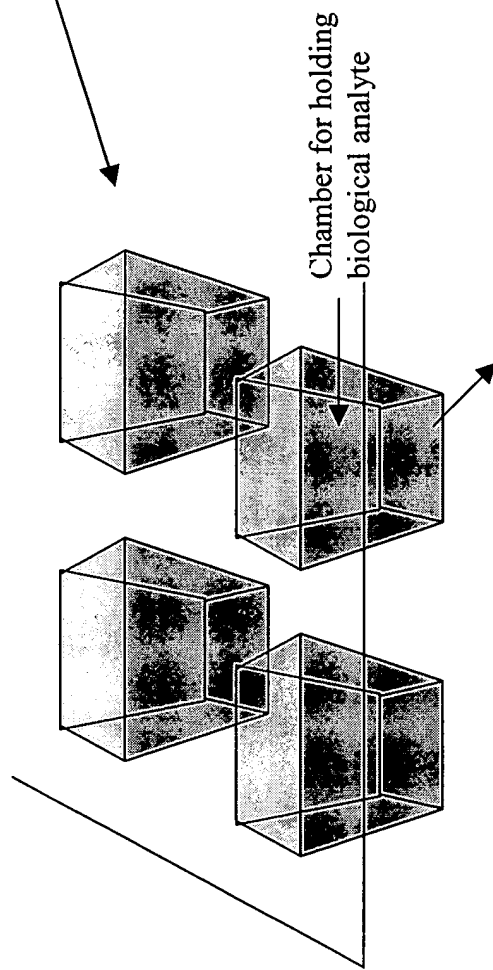
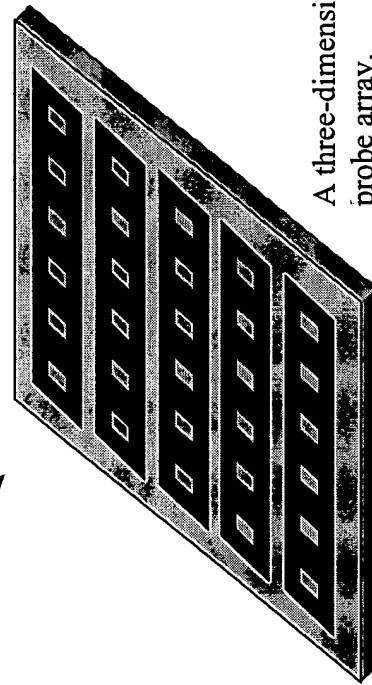


Figure 20B.



A three-dimensional
probe array.

Figure 20C.

Another implementation of Inverted array device, where the array on each inverted structure is a 3D porous array

The microarray biochip can also be housed in a sealed hand-held or Point of Care device.

Figure 21A.

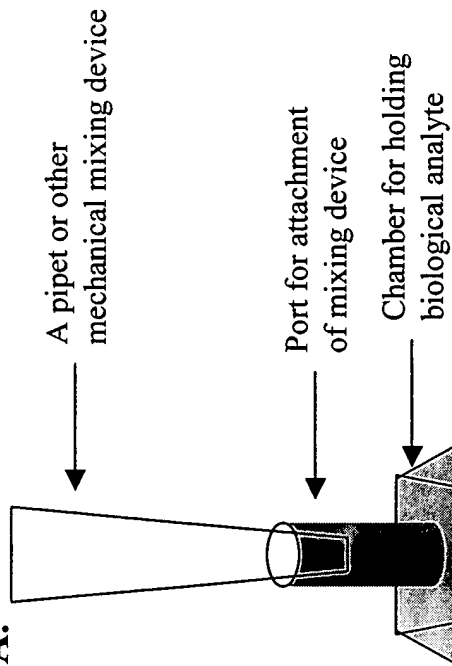
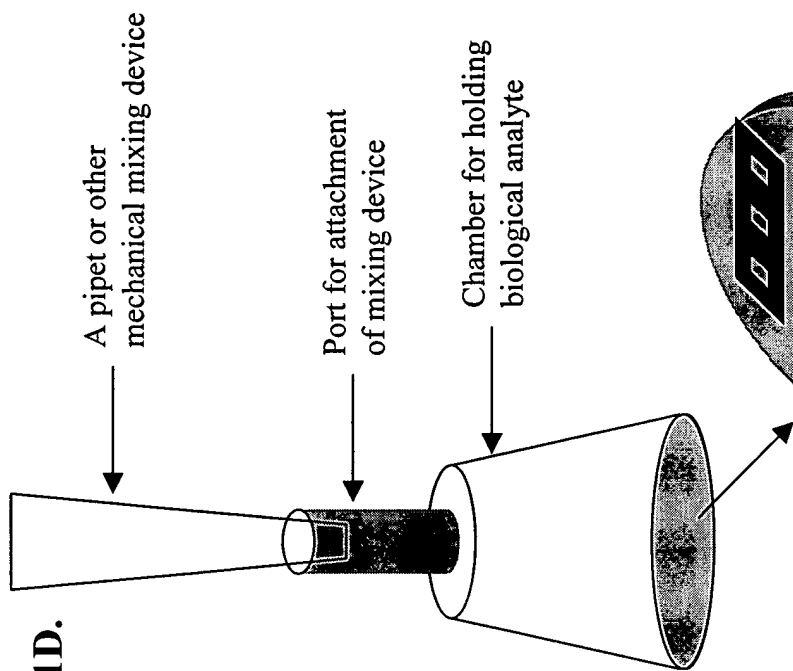


Figure 21D.



A three-dimensional probe array.

Figure 21B.

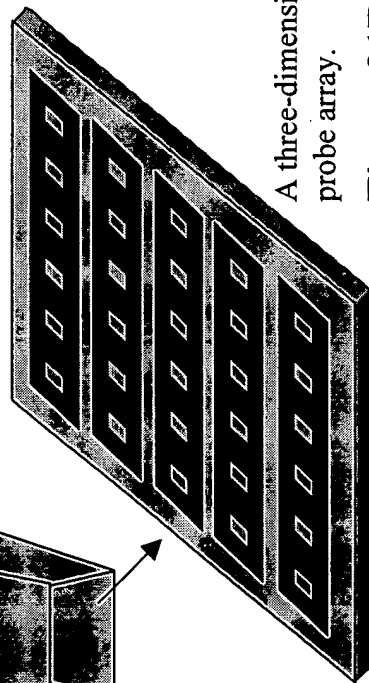
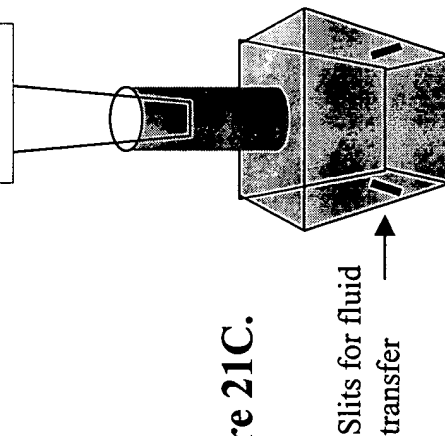


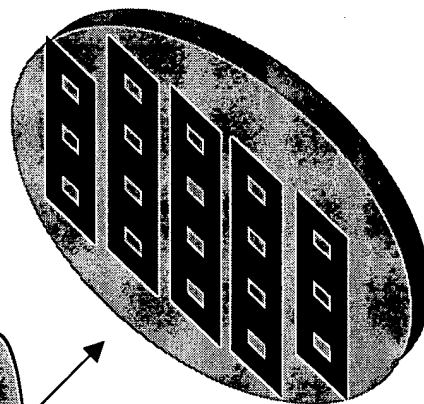
Figure 21C.



Another implementation of the chamber for holding biological analyte

A three-dimensional probe array.

Figure 21E.



Each array in the central microfluidic chamber can have one or more probes attached to it. The probes can be attached using either stable or cleavable linkers. Cleavable linkers can help move the probe-target complex to the adjacent chamber for secondary analysis.

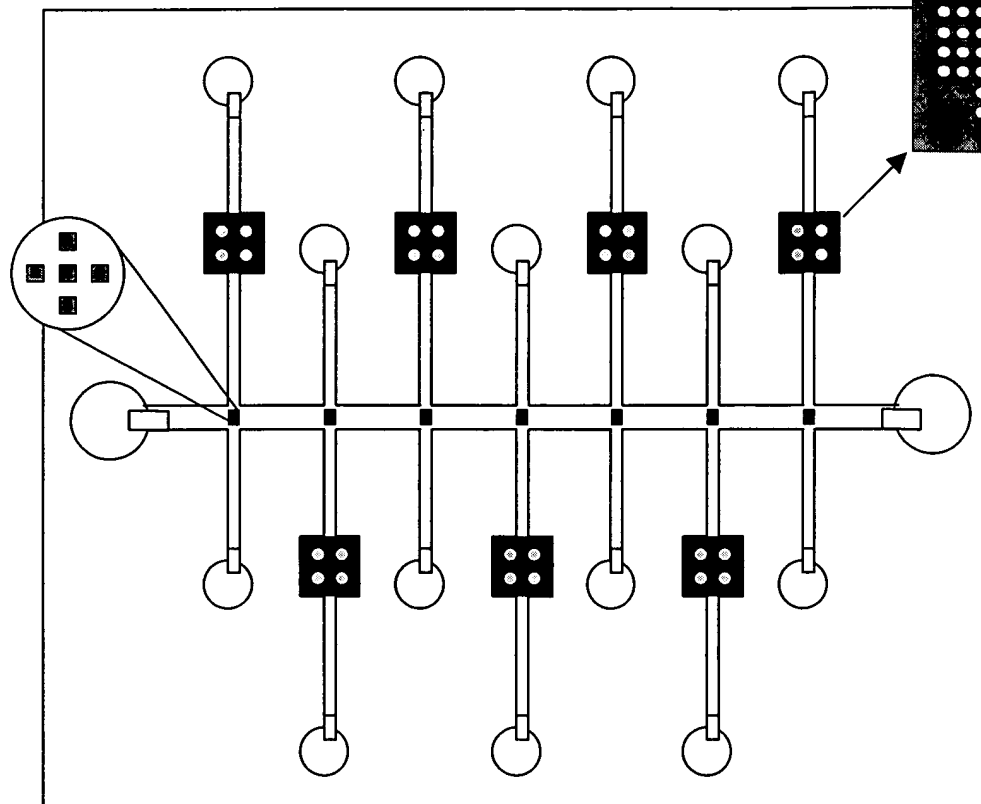


Figure 22A.

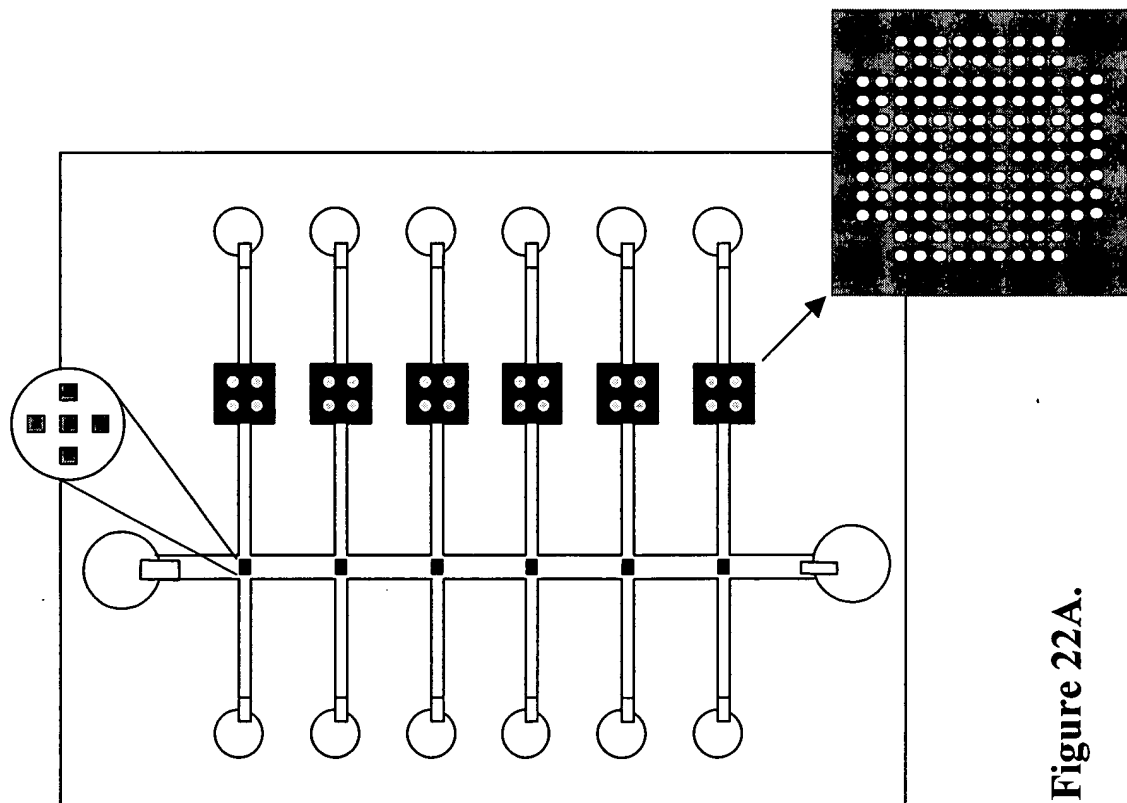


Figure 22B.

A microfluidic microarray and microchannel combination chip for multiplexed analyses.

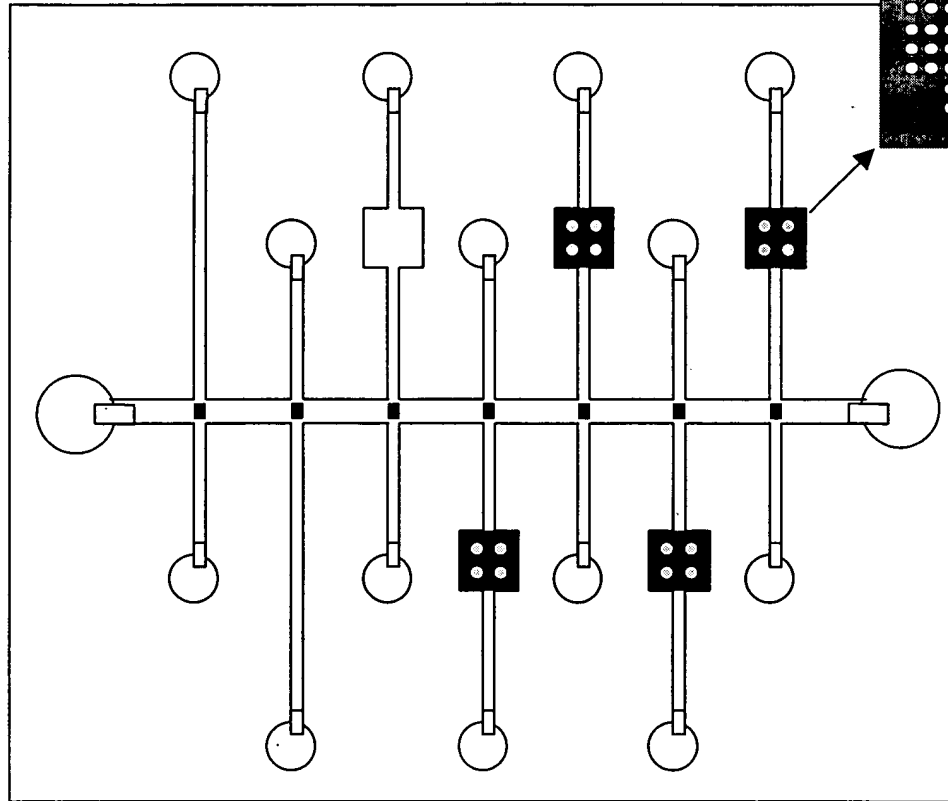


Figure 23A.

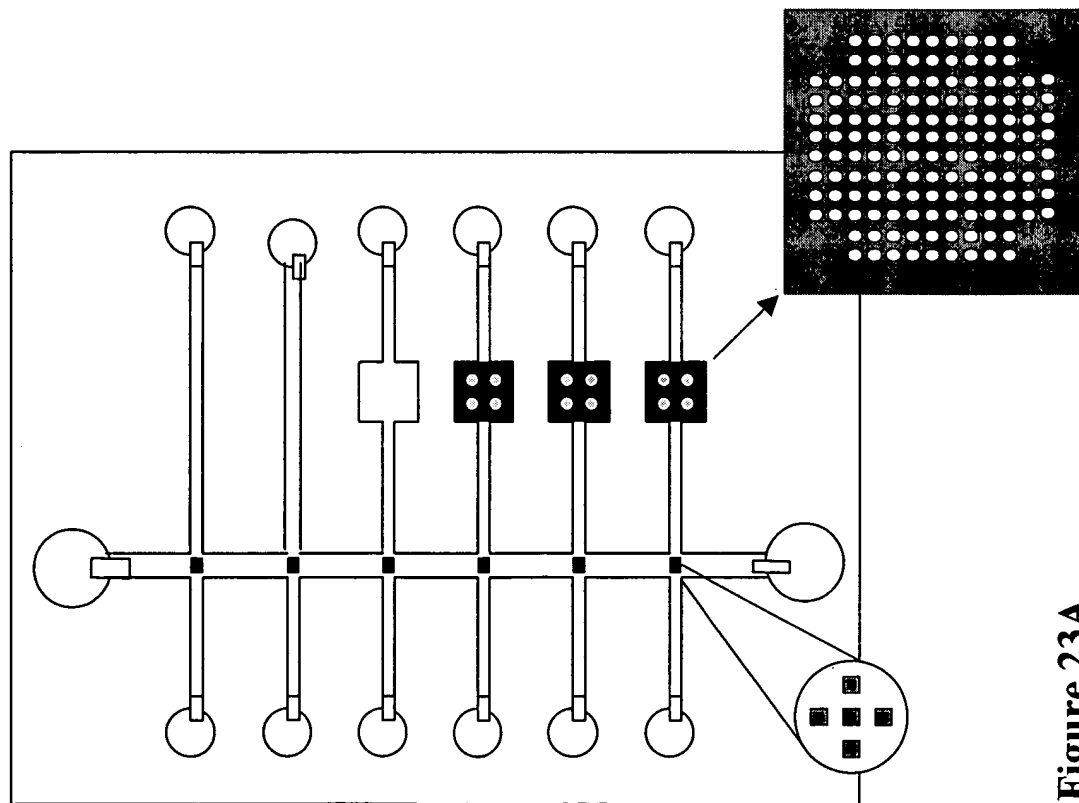
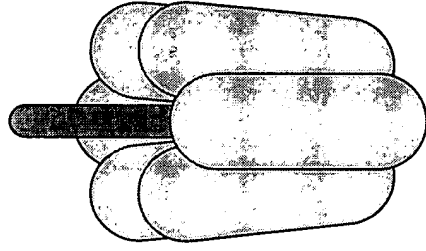


Figure 23B.

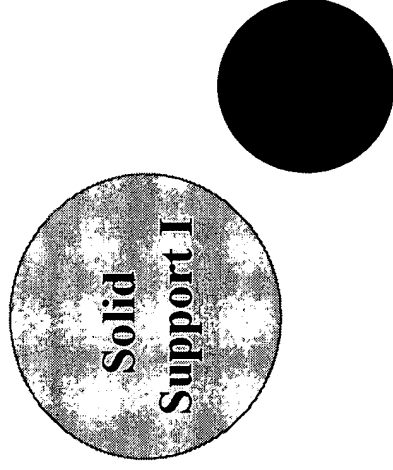
ATPase based Fluid-Micromixers

Figure 24A.



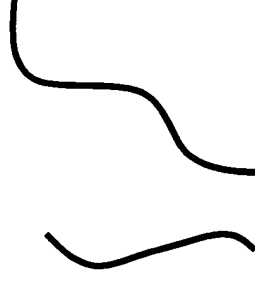
Cartoon of the multi-subunit enzyme – ATPase – that rotates in response to ATP synthesis to hydrolysis. The centrally located γ -subunit rotates relative to the hexameric α, β -subunit core.

Figure 24B.

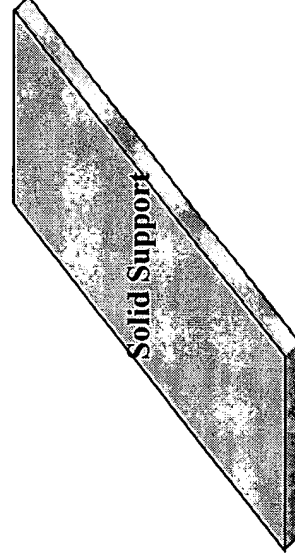


Spherical Beads as Solid supports for attaching different subunits of ATPase

Figure 24C.



Linkers for attaching different subunits of ATPase to the solid support

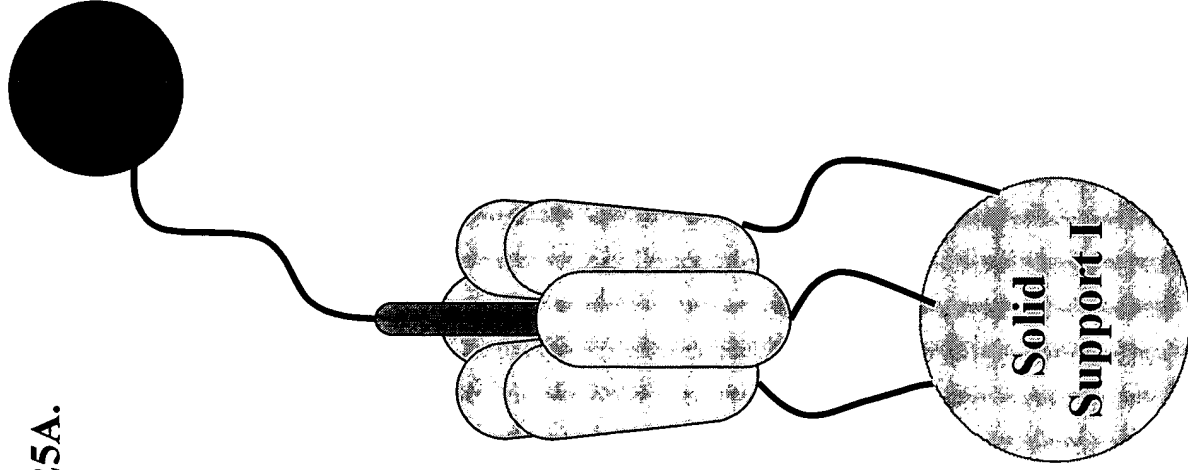


Flat platform base as Solid supports for attaching one of the subunits of ATPase

Figure 24D.

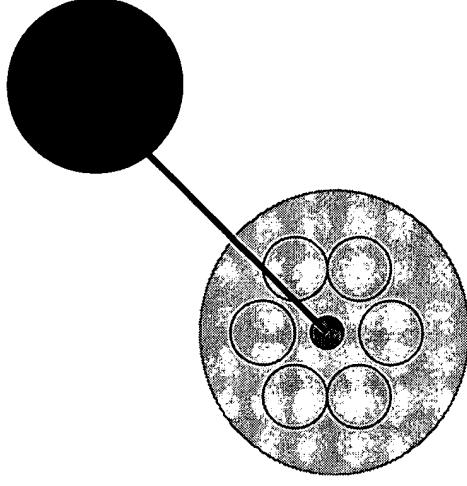
ATPase based Fluid-Micromixers, Model I

Figure 25A.



One particular implementation of ATPase-based fluid-micromixers. The γ -subunit and the α, β -subunit core are both attached to two different spherical beads.

Figure 25B.



A cartoon showing ATPase subunits attached to two beads from another angle.

A cartoon showing rotation of the two beads bound to ATPase (Model I micromixer) upon addition of ATP

Figure 26A.

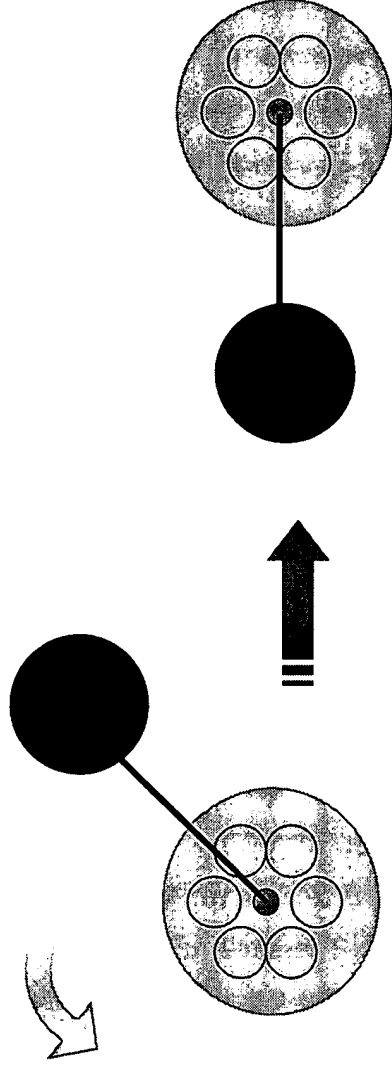


Figure 26B.

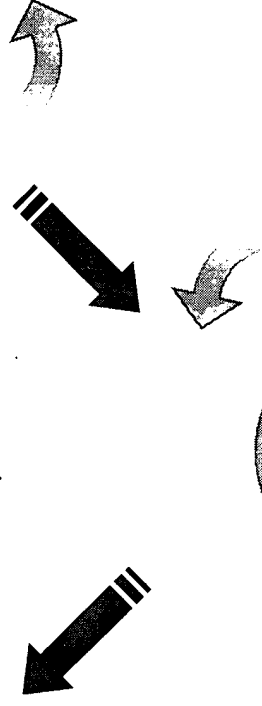
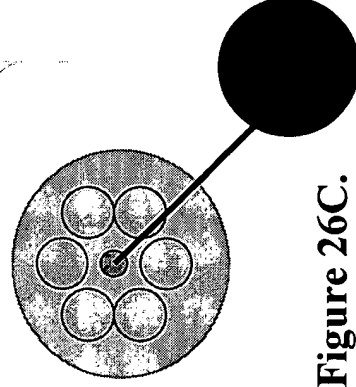
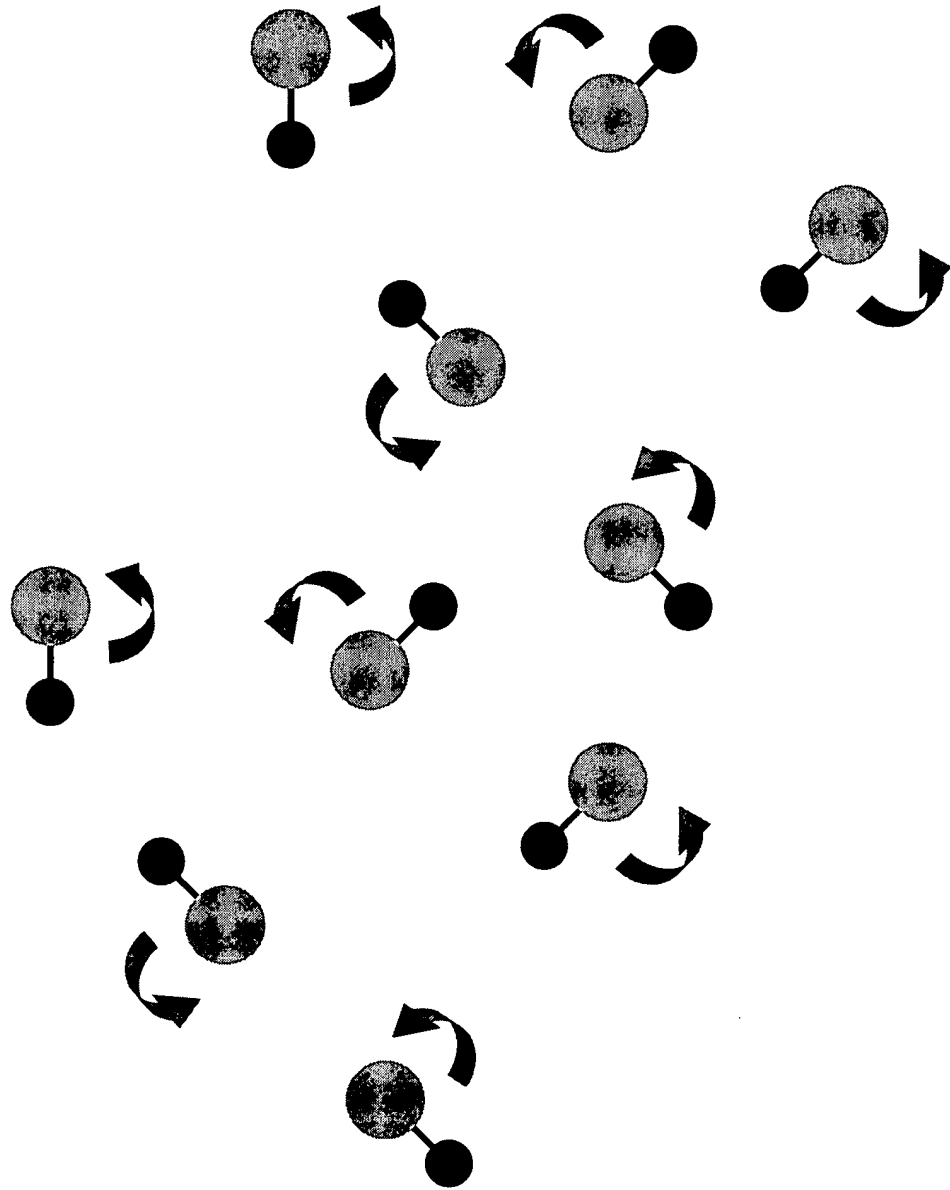


Figure 26C.



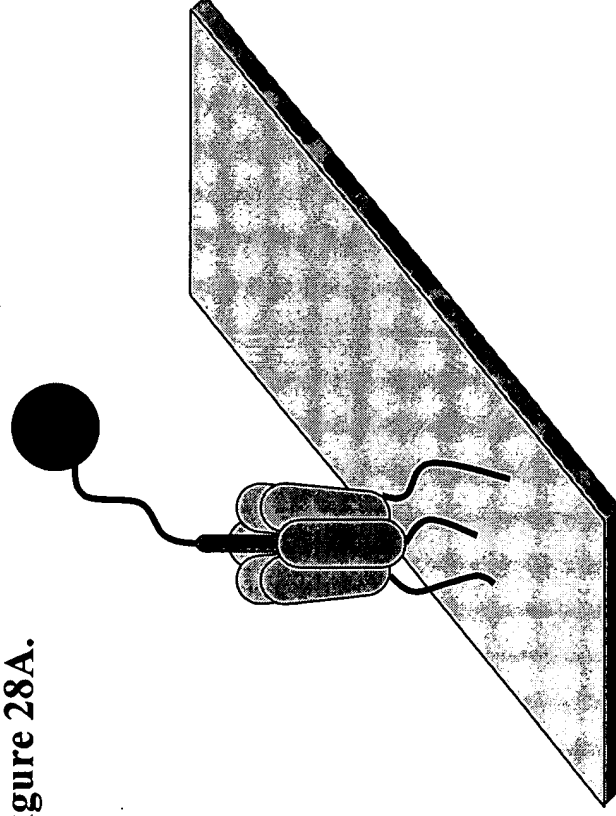
A cartoon showing multiple Model I Micromixers in action in a solution

Figure 27.



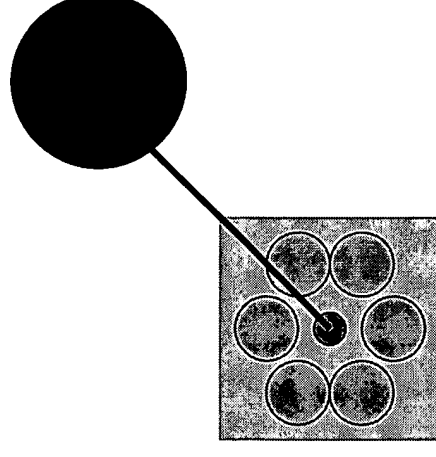
ATPase based Fluid-Micromixers, Model II

Figure 28A.



Another implementation of ATPase-based fluid-micromixers.
The γ -subunit is attached to a spherical bead and the α, β -subunit core is attached to a solid platform.

Figure 28B.



A cartoon showing ATPase subunits attached to two different surfaces from another angle.

A cartoon showing multiple Model II Micromixers in action in a solution

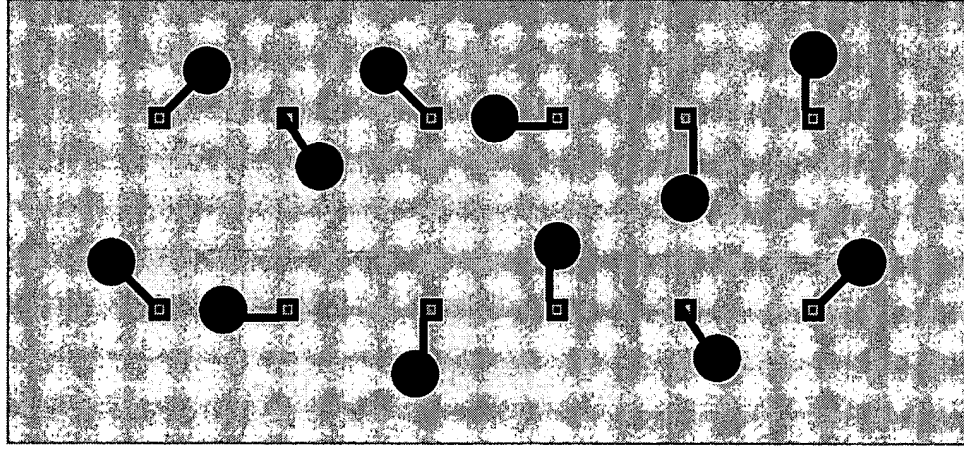


Figure 29.

All the mixers are moving in a counter-clockwise direction

Kinesin and Myosin based Fluid-Micromixers

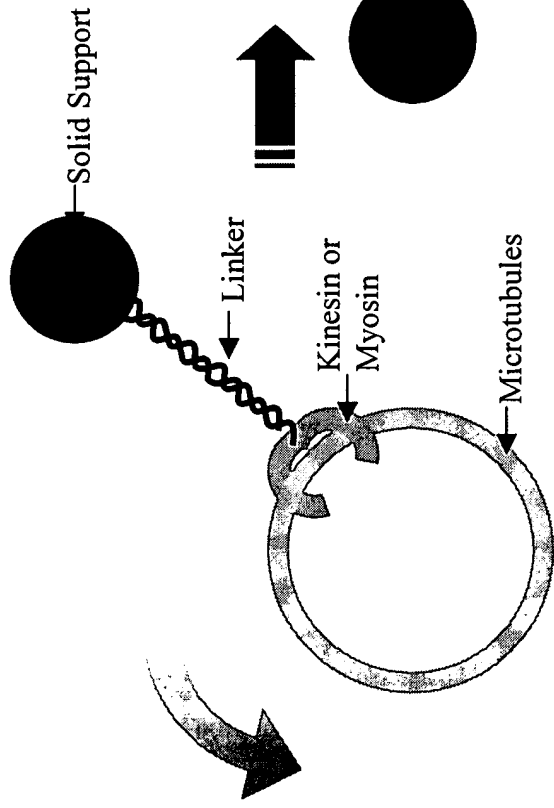


Figure 30A.

Figure 30B.

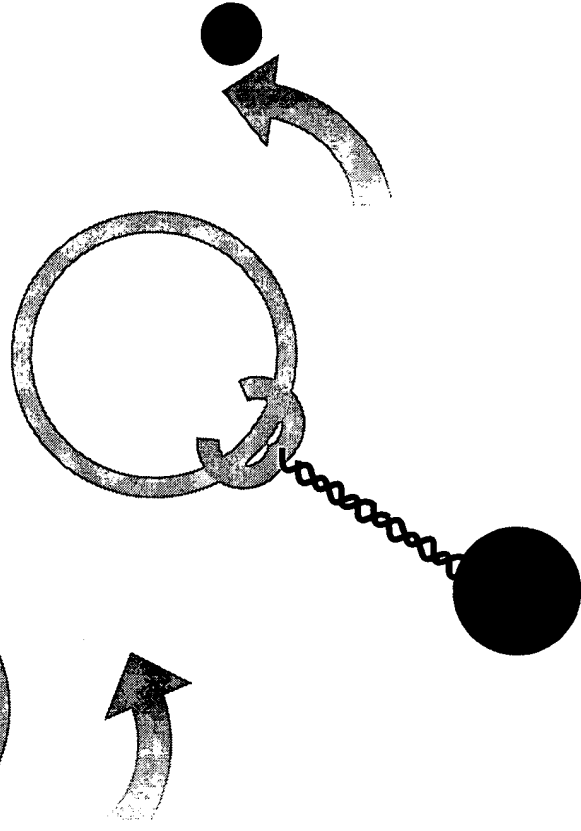
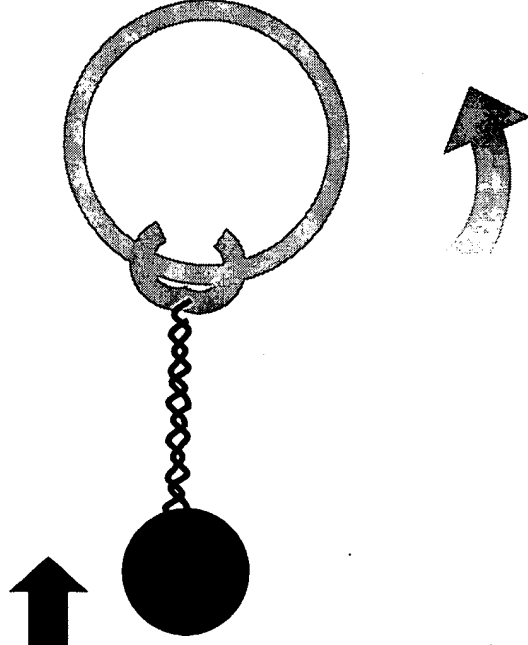


Figure 30C.

Figure 31 **Circular Triplex Forming Oligo (CTFO) DNA and Other** **Pseudo-rotaxane based Fluid-Micromixers**

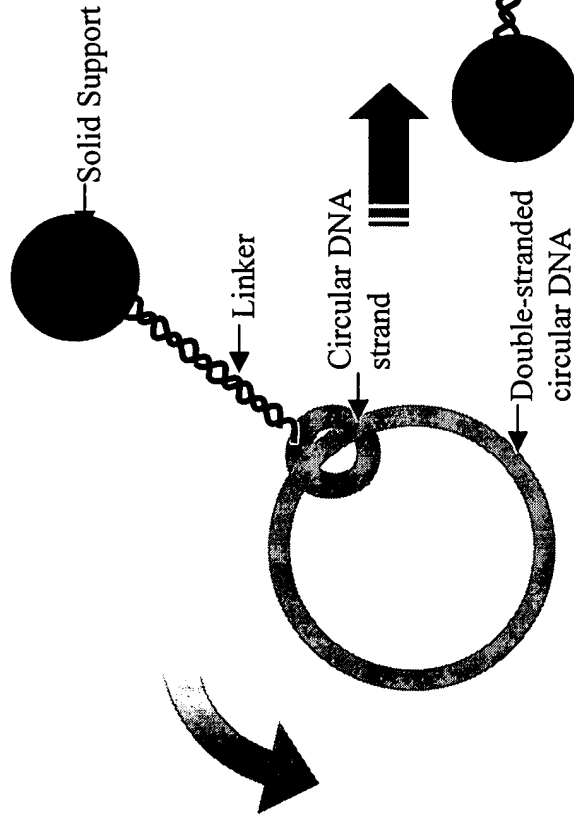


Figure 31A.

Figure 31B.

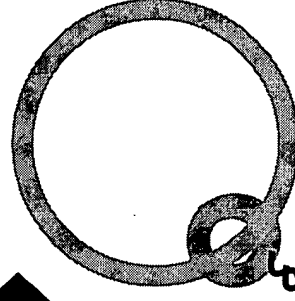
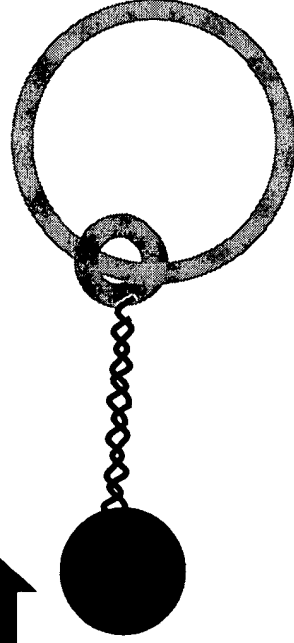


Figure 31C.

DNA Helicase and DNA Sliding Clamp based Fluid-Micromixers

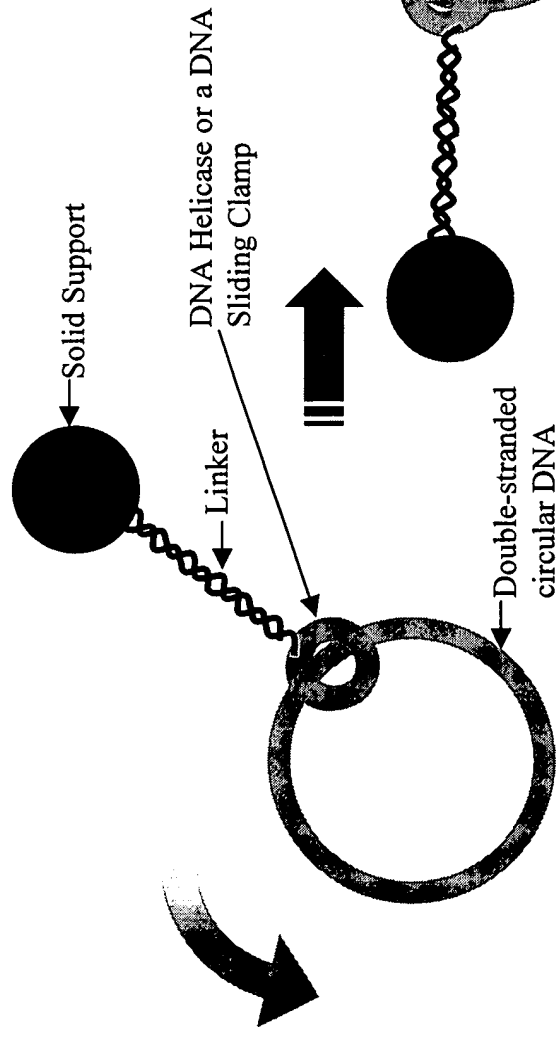


Figure 32A.

Figure 32B.

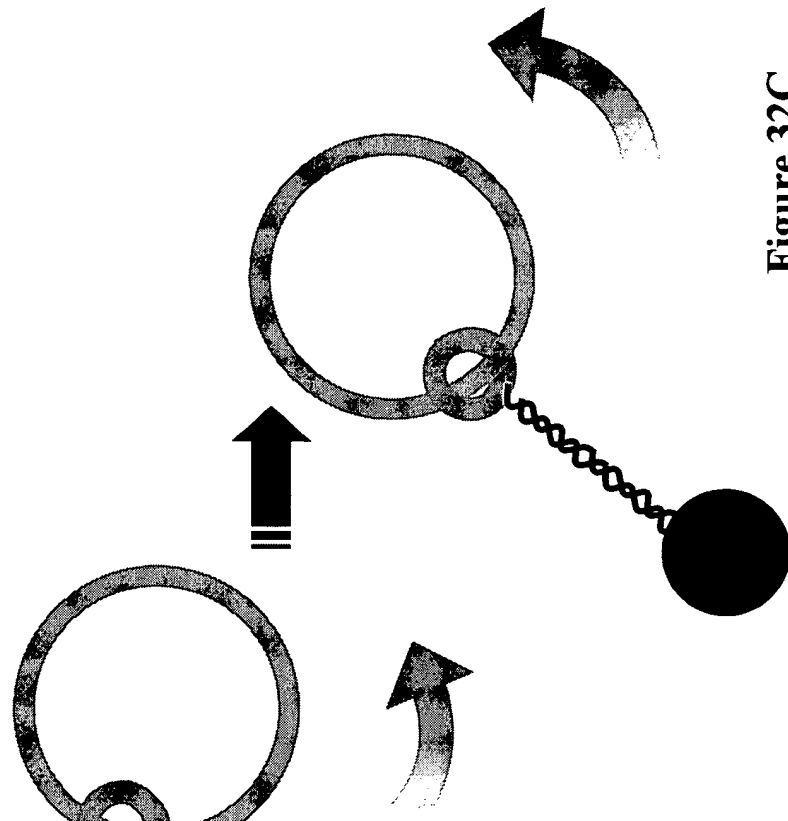


Figure 32C.

DNA Helicase (bound to Circular Triplex Forming Oligo (CTFO) or a Sliding Clamp) based Fluid-Micromixers

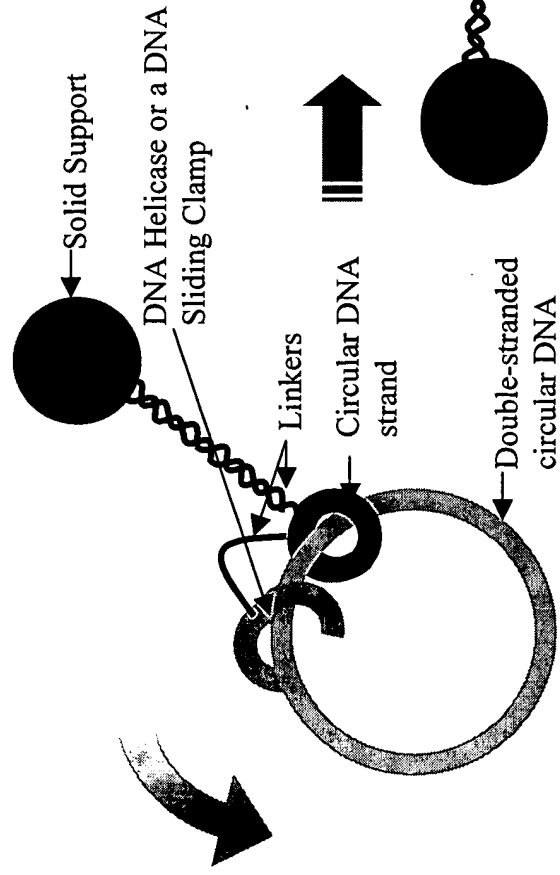


Figure 33A.

Figure 33B.

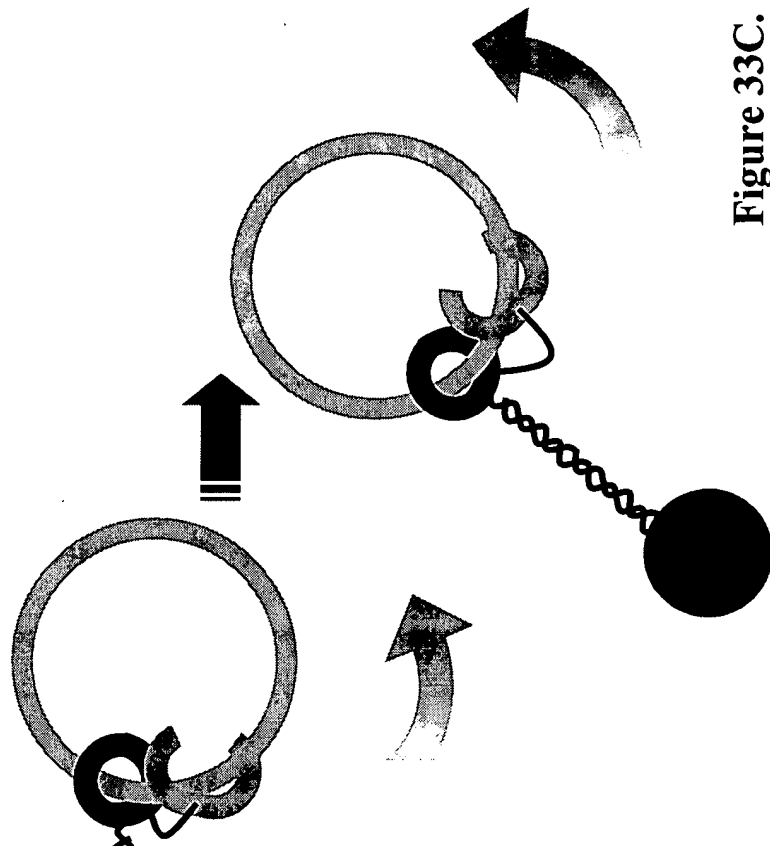


Figure 33C.

Hybridization Enhancement Using Strand-Invader Molecules

Figure 34A.

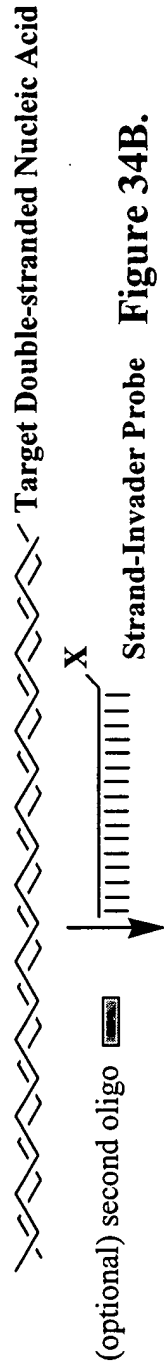


Figure 34C.



Figure 34D.

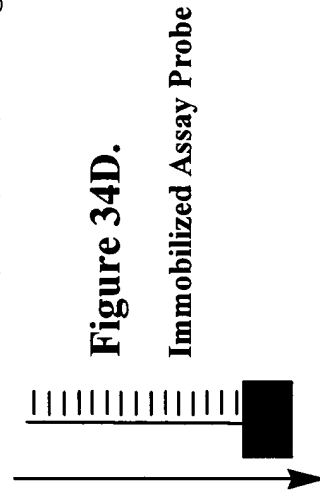
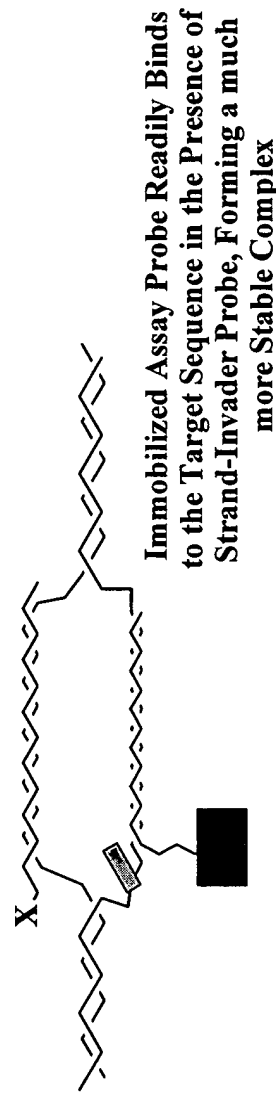


Figure 34E.



X = Optional Detector Moiety

A gasket/separator can be used in the current hybridization chambers to place two biochips facing each other in a single chamber for duplicate experiments.

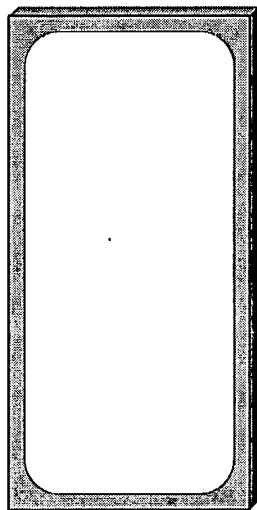


Figure 35A.



Figure 35B.



Figure 35C.



Figure 35D.



Figure 35E.



Figure 35F.

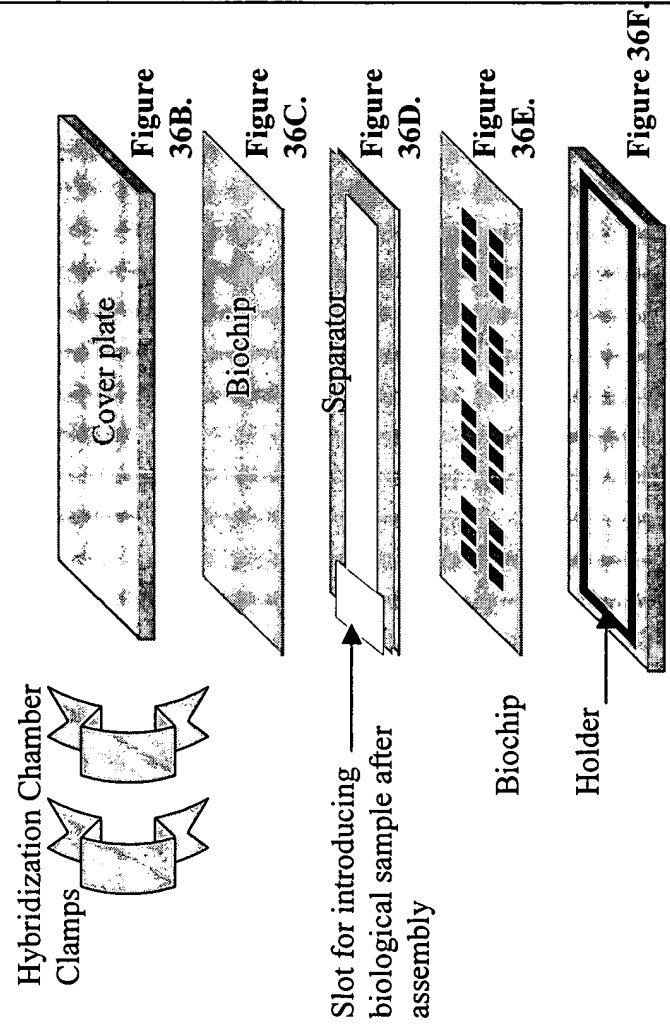
A sketch of one example of a new hybridization chamber.
A hybridization chamber can be devised such that it fits two biochips.

Figure 35G.



I. A gasket/separator can be used in the current hybridization chambers to place two biochips facing each other in a single chamber for duplicate experiments.

Figure 36A.



II. The separator can also be built into the chamber.

Figure 36G.

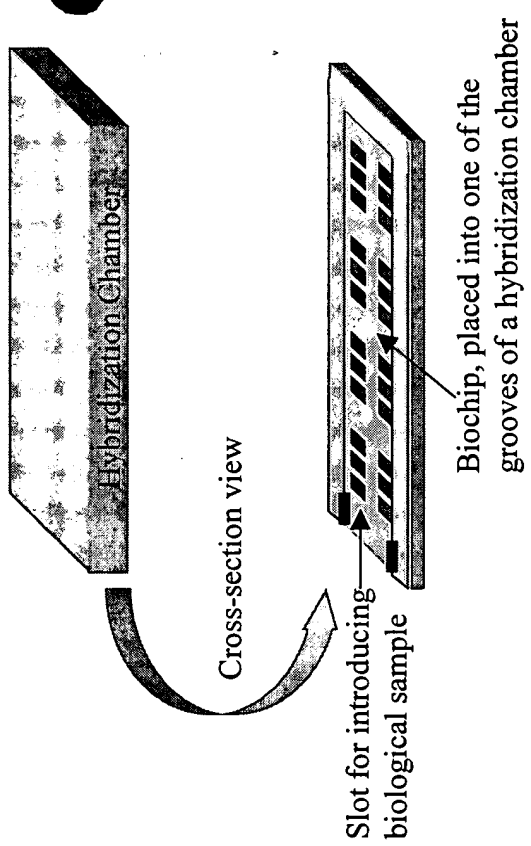


Figure 36H.

A sketch of two more examples of new hybridization chamber.

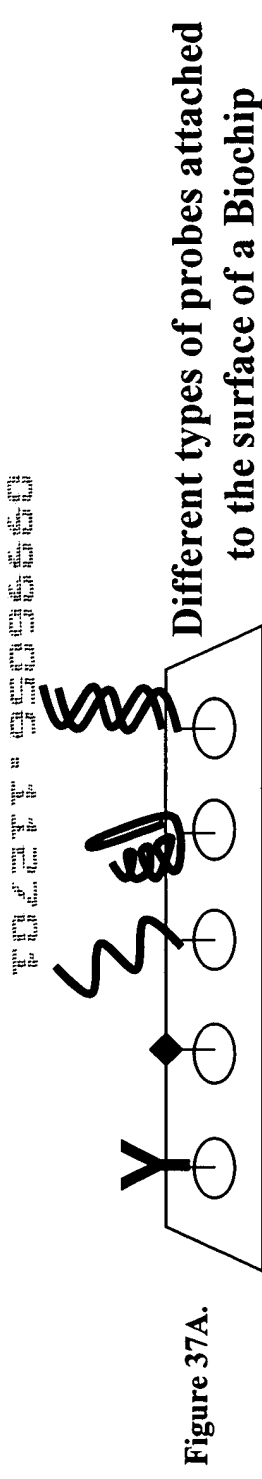


Figure 37A.

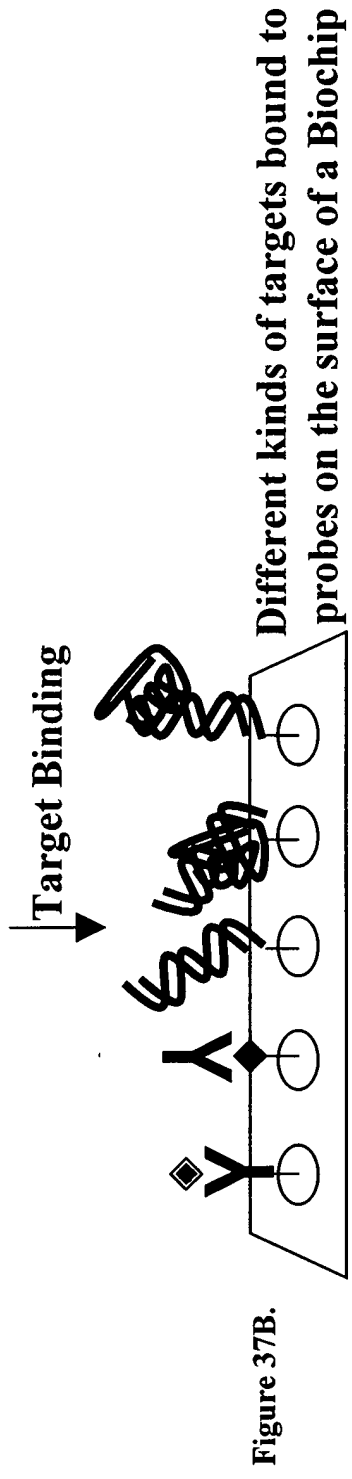


Figure 37B.

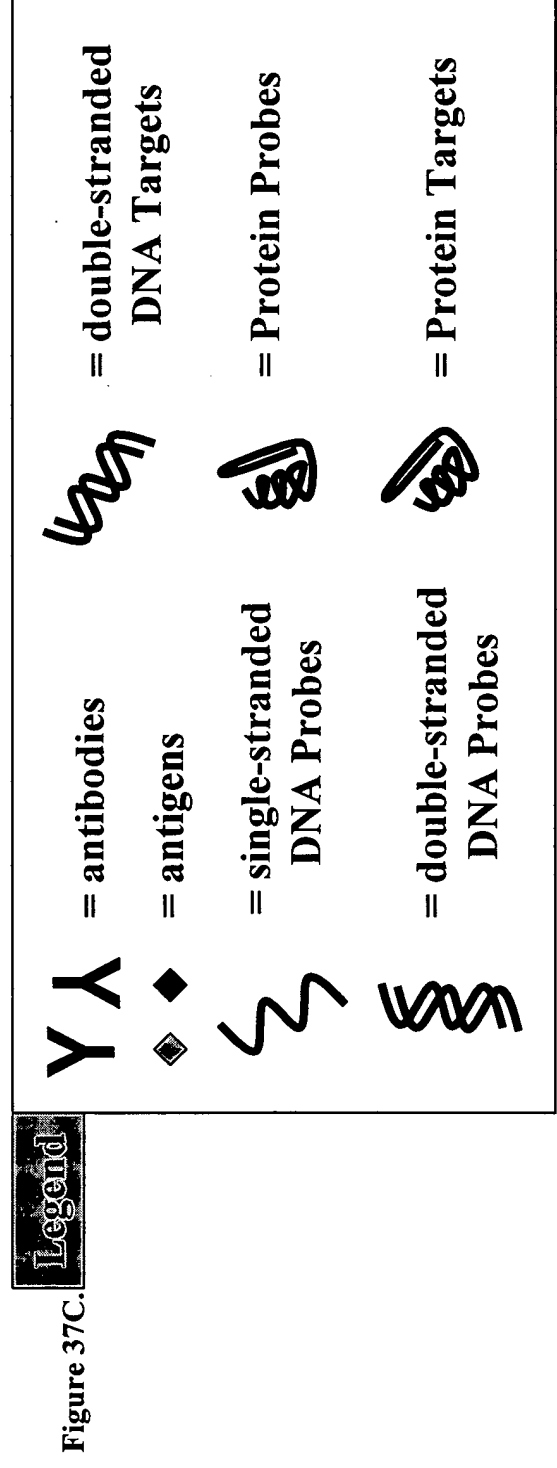


Figure 37C.

A schematic showing the principal behind the UniScreen Technology. It allows detection of any analyte – such as DNA, RNA and Proteins - in a single multiplexed assay.

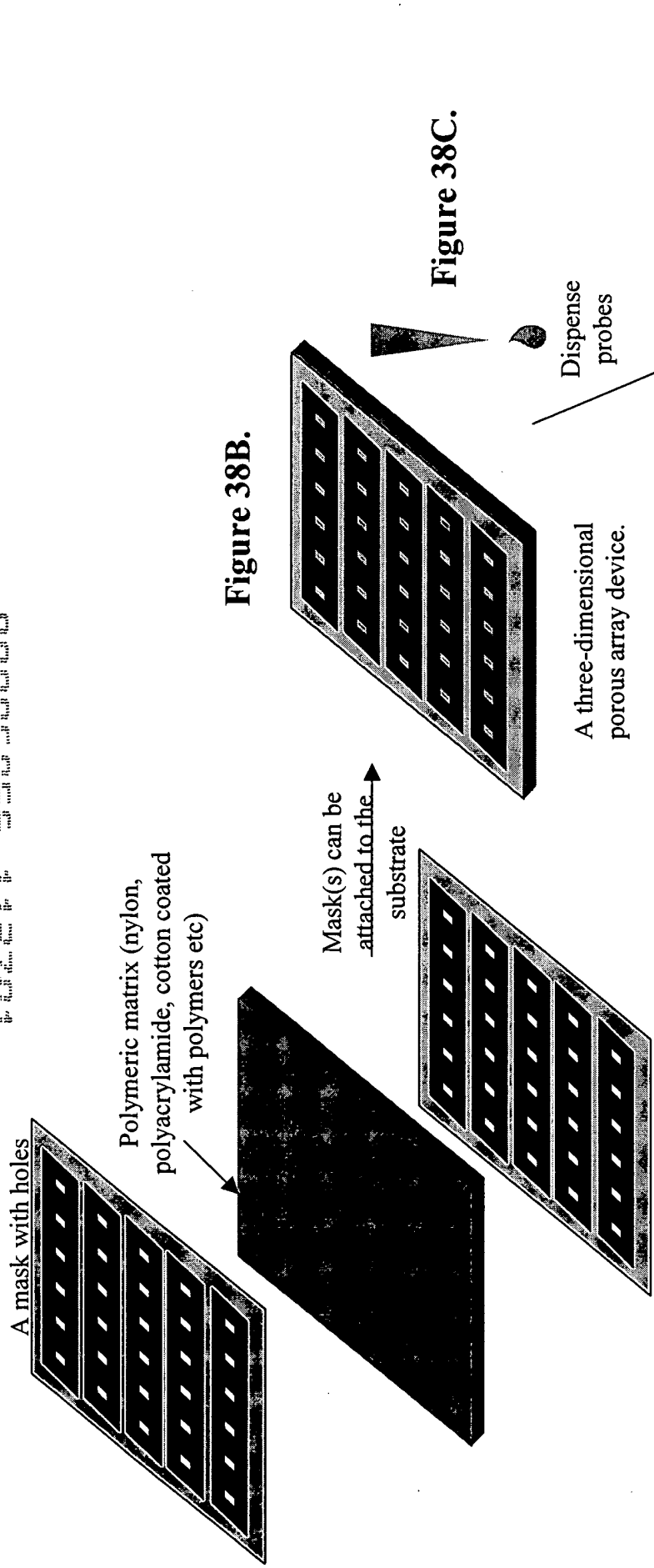


Figure 38B.

Figure 38C.

Figure 38A.

Figure 38D.

Probes can be dispensed on the porous substrate through the holes in the mask